BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

(THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL)

(SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY)

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William A. Brown
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Vol. XLI, No. 1 JULY, 1927

Contents

The Presentation of the Thayer Lectureship 1

A Contribution to the Study of Mycotic Warts. A. PENA CHAVARRIA, M.D., PH.D., AND P. G. SHIPLEY, M.D. 11

The Bactericidal Activity of Hexylresorcinol in Glycerine. With Special Reference to the Influence of Surface Tension in Chemical Disinfection. VEADER LEONARD, M.D., AND WILLIAM A. FEIRER, SC. D. 21

Heart Lesions Produced by the Deep X-Ray. An Experimental and Clinical Study. F. W. HARTMAN, M.D., ADOLPH BOLLIGER, PH.D., H. P. DOUB, M.D., AND F. JANNEY SMITH, M.D. 36

A Study of the Ovarian Follicular Hormone in the Blood of the Pregnant Woman. MARGARET G. SMITH 62

Book Reviews 67

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THE PRESENTATION OF THE THAYER LECTURESHIP

On the eighteenth of May 1927, there gathered at dinner in the Mayflower Hotel, in Washington, D. C., a large and representative group of colleagues and friends of Dr. William S. Thayer to present to the Johns Hopkins Medical School a lectureship in his honor, as a testimonial of esteem and affection.

Dr. Frank Billings of Chicago presided, made the opening address and introduced the speakers. Dr. Joseph S. Ames, Provost and Acting President, represented the University.

The address of presentation was made by Dr. Leonard G. Rowntree, being read in his absence by Dr. Roger S. Morris.

The deed of gift was then read: This provided that the principal sum (over sixteen thousand dollars) be held in trust by the University as an endowment for the "William Sidney Thayer and Susan Read Thayer Lectureship in Clinical Medicine," and that the income be used to provide one or more lectures annually in the Johns Hopkins Medical School, the lecturers to be selected from men distinguished in Clinical Medicine, Pediatrics, Neurology or border-line branches. That the choice of the lecturers and the expenditure of the income be directed by a committee composed of the incumbents of the Chairs of Medicine, Pediatrics, Neurology, and Pathology in the Johns Hopkins Medical School, the committee being empowered to expend the whole or any part of the income in any year, to allocate accumulated income, to increase the honorarium as occasion may demand, to make appropriate disbursements for the expenses and entertainment of the lecturers, or to return unexpended income to the corpus of the trust.

Provost Ames accepted the gift on behalf of the University and acting for the Trustees agreed to the conditions of the deed.

Dr. Billings then called for brief remarks from some of Dr. Thayer's old friends and associates. Informal addresses were made by Dr. Simon Flexner, Dr. J. M. T. Finney, Dr. Thomas McCrae, Dr. T. B. Futcher, Dr. Lewis A. Conner, and Dr. Charles Minor.

Dr. William S. Thayer, who was greeted with acclamation, then

BULLETIN OF THE JOHNS HOPKINS HOSPITAL, VOL. XLI, NO. 1

made acknowledgment to his friends present and absent for the great honor and pleasure they had bestowed upon him.

Dr. Frank Billings as chairman said:

Ladies and Gentlemen:

We, a few of the many friends of William Sidney Thayer, have assembled here to express in a practical way our sincere and heartfelt appreciation of him and his life's work.

As chairman of the committee organized to secure a Thayer lectureship fund, and honored furthermore by the permission to preside at this banquet, I shall presume upon your good nature to express my individual sentiments in regard to our guest.

It is just thirty years ago that I met Dr. Thayer in Moscow, Russia, where we were in attendance on the International Medical Congress. There were a good many Americans in attendance at this meeting including General Sternberg, Nicholas Senn, Dr. Lewellys F. Barker, the late Henry B. Favill and others. The opening meeting was held in the opera house, a magnificent building, and was presided over by one of the Grand Dukes. All nations taking part in the Congress were represented by speakers appointed by each country at the opening meeting. Dr. Thayer represented the United States and made all of us proud of him and of our country by the splendid address made with all the becoming modesty of the man.

Since that time our acquaintance of thirty years ago has ripened into a real friendship, characterized by respect and real affection on my part, which I am happy to believe is reciprocated.

All of us have noted his splendid qualifications as a physician, clinical investigator and teacher and the steady and progressive development of the man. We know that he is a patriotic and conscientious citizen. Ten years ago when the federal government decided to send an American Red Cross Mission to Russia, I was authorized to make selection of the professional members of the Mission. I requested Dr. Thayer to join the Mission and at first he hesitated because of the serious illness of his beloved wife. That noble woman, appreciating the fact that Thayer could and would give splendid service to the people of Russia as a member of the Mission, urged him to accept membership on the Mission because she knew it would make him happy; and we have it evidenced that this sacrifice on her part gave her great satisfaction and joy, even though she knew at the time that with his going it was probably a last farewell.

On that long journey to Russia and the close association necessary in the work done, I came to know Thayer thoroughly and well. He proved that he possessed initiative, purposeful energy, a cooperative spirit, and his work contributed largely to the success of the work of the Mission.

We received a cablegram in Russia announcing the passing of the spirit of Susan Read Thayer. With broken heart his indomitable spirit carried Thayer

forward in the efficient work which all deemed necessary to fulfill the object of the Mission in Russia.

Thayer has an open mind. He is ready and willing to listen to the opinion of others and to modify his own when he is convinced that others are right; but when assured by his ever active conscience that he is right in his opinion, he stands as steadfast as a rock in justification of himself.

He is a manly man and, with all, has a deep and sincere sympathy for the afflicted and has proved himself a true and helpful friend.

About a year ago Dr. Leonard G. Rowntree, a student of Dr. Thayer, whom we all respect and are delighted to know, conceived the idea of honoring Dr. Thayer by the establishment of a Thayer Lectureship Fund. Dr. Rowntree communicated with Dr. Roger Morris who heartily agreed with him in the project, and together they organized the committee on invitations to the friends of Dr. Thayer to join in this project to do him honor.

It was planned to have Dr. Rowntree present the fund collected to the representatives of the Johns Hopkins University tonight. You will all join with me in the regret that Dr. Rowntree is not able to be with us and will sympathize with him in the illness of his daughter and his wife which prevents his attendance.

Dr. Roger Morris, who as secretary-treasurer of the committee has greatly contributed to the success of the undertaking, will now read the presentation address prepared by Dr. Rowntree.

PRESENTATION ADDRESS PREPARED BY DR. LEONARD G. ROWNTREE

Mr. Chairman, Ladies and Gentlemen:

This is a delightful occasion, one that brings happiness to us all. From our point of view, it is so much more satisfactory to show appreciation to Dr. Thayer while he is still alive and active. From his point of view, the advantages must be more than obvious.

Dr. Thayer: We, your friends, former students, associates on the faculty and your many admirers have gathered here this evening from the length and breadth of the land to render grateful homage to you. We come because of our love and esteem for you and feel that it is but fitting and proper that you should know what you and your life have meant to us. To the world at large you are a great medical leader; to the medical profession, a great physician; to your colleagues, a great inspiration; to your students, a great teacher; but to us you are all these and more, a true friend, a man we trust and revere. We welcome this occasion to show you in a tangible, albeit inadequate way, the nature of our feeling for you.

As a physician your life has been rich in experience and full in achievement. You have participated, from its very beginning, in the growth of a great institution. In less than half a century, the Johns Hopkins Medical School has become recognized throughout the entire world for leadership in medical thought and medical practice. In this development you have played an important and prominent part. Yours has been the happy lot to enter its portals as a house officer, to

serve in your early days as an associate of the immortal Osler, to become a recognized leader at Hopkins and finally to be chief of its department of medicine. You have served Hopkins well, and it in turn has honored you. We recognize that through your productive scholarship, your personal attributes, and your kindly leadership you have contributed largely to its renown.

In making this presentation, we have but one regret, and that is that Mrs. Thayer, whose name is associated with yours in the lectureship to be created, is not here to rejoice with you and with us. Towards her we feel much as we feel toward you. I doubt if there is a single Hopkins student, who, in thinking of you, does not include Mrs. Thayer in the mental picture, and the gracious welcome of your home at 406 Cathedral Street. In rendering homage to you we rejoice that we may also honor her.

Mr. Provost: The history of an institution, like the history of a country, is the story of its great men. When we read the history of any great medical school, it is not the buildings, the wards, or the laboratories which interest us, but the men who have labored within its walls. We believe that in the future, when the story of the early years of the Johns Hopkins Medical School is being related, the life and work of Dr. Thayer will constitute one of its most interesting chapters.

The steps in the career of the present Emeritus Professor of Medicine of the Johns Hopkins Medical School are familiar to us all. He was born in Milton, Massachusetts, June 23, 1864. After graduating at Harvard, he studied in Vienna and Berlin. In 1891 he became resident physician of Johns Hopkins Hospital, and held this position until 1898. He was made Associate in the Johns Hopkins Medical School in 1895 and Associate Professor in 1896. He was Professor of Clinical Medicine from 1905 to 1918, and was finally Physician in Chief from 1918 to 1921. He has been the recipient of many honors in this country and abroad.

During the late war he was a Brigadier General of the Medical Corps and Chief Consultant of the Medical Service of the A.E.F., and was also awarded the distinguished service medal. He has been a member of the National Research Council, President of the Congress of American Physicians and Surgeons, Honorary President of the International Medical Congress in Moscow and in London, President of the American Association of Physicians, President of the Society of Tropical Medicine. He has served for years as a member of the Judicial Council of the American Medical Association, and holds the unusual distinction of being a member of the Board of Overseers of Harvard University while a professor at the Johns Hopkins Medical School.

His chief scientific contributions have been to our knowledge of parasites, the etiology of malaria, the changes in the blood in pathologic states, particularly in typhoid fever. He has been a productive student in the field of cardiac and vascular diseases, of chorea, of endocarditis and arteriosclerosis. He has shed light on the Adams-Stokes syndrome, and heart block, on the nature and significance of heart sounds and of cardiac murmurs. He has become eminent as a teacher investigator, clinician and author.

He has contributed largely to the success of the Johns Hopkins Medical School, not only in scientific achievement, but in the spirit of the institution. In honor of Dr. Thayer, and in behalf of those present and of all who have contributed to this foundation, I take great pleasure in presenting, through you, our gift to the Johns Hopkins University. It is our wish that this fund be used to create a lectureship to be known as the William Sydney Thayer and Susan Read Thayer Lectureship in Clinical Medicine.

May I add, sir, that in presenting this gift, our pleasure is two-fold, for in paying a tribute of love to Dr. Thayer, we are also expressing our appreciation of the great influence of the Johns Hopkins University. It is our hope that Dr. Thayer may long be spared for further service in this great institution. His inspiring and kindly influence, we know, will always continue to be felt at the Johns Hopkins Medical School.

Dr. Billings introduced Provost Ames who said:

It is a great privilege to have the honor of representing the Johns Hopkins University this evening, and President Goodnow regretted extremely that he could not himself be present. Before saying the few formal words on behalf of the University, which I shall say in a few moments, I beg permission to express as briefly as I can why the University feels so highly honored in having associated with it for all the years to come the name of Doctor Thayer.

Dr. Thayer is a great physician and a wise teacher. Others, with more personal knowledge than mine, will testify to these facts, I am sure, although I too know from my own experience what a wise, observant, sympathetic physician he is, and how grateful to him everyone is who has received his professional care. But his ability as a physician and investigator and his talent as a teacher do not at all account for our feelings towards Dr. Thayer, nor why we delight to do him honor. He has certain qualities which make us love him and trust him. As a man he is so full of human kindess, so generous, so unselfish, so pure of heart that when one even thinks of him there is a thrill of happiness in knowing there is such a man. He is so sympathetic with our human natures, and yet so fearless in word and action against injustice or meanness, and so brave morally and physically. It is no wonder that he has the affection of all who know him. But, more than this, he has, in its highest sense, character. I heard a man once say that he would entrust his immortal soul to Billie Thayer. So would I, with full confidence that in his keeping it would be safer than in my own. He inspires instant, absolute confidence.

It is for these reasons, and others I could give, that the Johns Hopkins University is honored by having a lectureship bearing Dr. Thayer's name permanently endowed in its Medical School. You friends of Dr. Thayer have chosen a wise method of showing him honor; for you wish his name to be known by countless men in the future and you wish these men to know your own respect and admiration for him. Of all the institutions resulting from man's activity, nothing on this

earth seems to be as permanent as a University, and a lectureship in one does grant immortality to him whose name it bears.

It is a particular pleasure to all of Dr. Thayer's friends that in this lectureship the name of his wife is associated with his. To all who knew that gracious lady, her spirit, her bravery, her brilliant mind form a treasured memory.

I have been given authority by the President of the Board of Trustees of the Johns Hopkins University to accept this gift of the friends of Dr. Thayer under the conditions specified for the endowment of the "William Sydney Thayer and Susan Read Thayer Lectureship on Clinical Medicine." I beg to thank these friends through you, Mr. Chairman, but, above all, to thank Dr. Thayer for having by his life inspired such love and respect.

Dr. Billings introduced Dr. James B. Herrick, who said:

In the three minutes assigned to me I desire to refer to two points.

First to Dr. Thayer as a lover of books. Whoever hears him talk, or reads what he has written either in medical or polite literature, knows that Thayer has held converse with the best of the world's great minds as revealed in their writings. To see him in his library lovingly turn over the pages of a choice first edition enables one to understand the spirit that induced Charles Lamb reverently to kiss an old folio. Only duty or the call of the wild can entice Thayer away from his books. The cry of the wild duck in the reedy cove down the bay, the leap of the trout in the mountain stream, the majestic silence of the primeval forest, these have a lure that is not to be resisted. He may say with Chaucer:

> On bokes for to rede I me delyte,
> And to hem yeve I feyth and ful credence,
> And in myn herte have hem in reverence
> So hertely, that ther is game noon
> That fro my bokes maketh me to goon,
> But hit be seldom, on the holyday;
> Save, certeynly, whan that the month of May
> Is comen, and that I hear the foules singe,
> And that the floures ginnen for to springe,
> Farwel my book and my devocioun!

Then, early to the fields to see the flowers, particularly the daisy, unfold their beauties to the rising sun.

The love of books and of nature keeps the mind clear and the heart pure.

The other point. Dr. Thayer with his refinement, his kindliness, his gentleness, his almost womanly tenderness, yet has in him the sterner stuff of which heroes are made. He has courage. He can face physical danger. He can stand for the right. He is willing to sacrifice self and life's choicest pleasures for duty. Like a knight of King Arthur's Round Table his vow might well have been

To ride about redressing human wrongs.
To honor his own word as if his God's.
To love one maiden only, cleave to her,
And worship her by years of noble deeds.

Or, like the well-known Knight of the Canterbury Prologue, he is

a worthy man,
That fro the tyme that he first bigan
To ryden out, he loved chivalrye,
Trouthe and honour, fredom and curteisye.

And of his port as meke as is a mayde.
He never yet no vileinye ne sayde
In al his lyf, un-to no maner wight.
He was a verray parfit gentil knight.

I leave you the thought of Thayer the lover of books and of Nature, the "verray parfit gentil knight."

Dr. Billings said:

And now William Sidney Thayer, may I say to you on behalf of your friends present at this board and absent, that it has been a joy and privilege to participate in this deserved honor to you. We hope it will be forever an index of your worth as physician and man to the members of our profession who follow us; we need no such reminder, for you will live forever in our minds and hearts.

Dr. Thayer said:

My dear Master, Friends:

What can I say! I cannot adequately express what I feel; I shall not try to. I can however tell you how happy I am that you should have made this a lectureship on clinical medicine to which most of my life has been given. You may not all know that at the beginning of my career and for many years afterwards, my desire was not to be a clinician but to be a pathologist. My one wish was for opportunity to work on special problems in the pathological laboratory. A good deal of my time in the Medical School, especially in my second year, was spent in the pathological laboratory. During my year in the Massachusetts General Hospital I made a number of the autopsies for the medical side, and during my year in Europe it was in the pathological laboratory that I spent much of my time. But I had debts and I had to earn my living; and so in September 1890, when I returned to Boston, I opened a consulting room at 86 Charles Street. This consisted of a small hall reception room with an alcove containing a set washbasin. It was a tiny room with a desk, which is now desecrated by my associate Rutledge in the laboratory, a few chairs, some sort of a couch for the ex-

amination of patients, and a beautiful structure resembling a bookcase, which on touching a mysterious spring suddenly expanded into a bed. My clientele—I had two patients in three weeks of practice—was expected to wait in a rather dingy hall. My consulting room was next door to an African Methodist Episcopal Church, which was on the corner of Mt. Vernon street. It was pointed out to me that the situation was unusually advantageous, as the patient or distracted friends rushing around the corner would stop at the first doctor's sign. Such indeed was the history in the case of one of my two patients.

I had been lucky enough to gain an appointment as Visiting Physician to one of the districts of the Boston Dispensary, but dreamed of Baltimore where the great new institution had been opened, to which already my two surgical associates, Finney and Phippen, had gone. One evening a friend called on me. He had been my junior on the medical service. He had come to say good-bye; he was sailing in a few days for Europe. After a pleasant talk we shook hands and went to the door. Before opening it he struck a match, lighted a cigarette, started out and then said "Oh, by the way, I wonder if you know some man who has just finished his hospital interneship who would care to go to the Johns Hopkins Hospital to take a position in the Medical Service. So far as I can make out the work is a good deal the same as that done by John in the out-patient department, namely, to look over the patients as they come in and direct them to the various departments where they belong. He is called 'differentiating physician.' He works in the medical out-patient department in the morning, spends an hour 'differentiating' in the afternoon, and has the rest of his time for his own work. He will live in the hospital and be a member of the staff." Dr. Osler had offered him the position, but he had been advised that it would be better for him to have his European experience first. I asked him immediately when he must have his reply—"Will tomorrow do?" "Oh yes" said he "there is no hurry." "Well," said I, "I would like to talk the matter over with my father." At this he took the cigarette from his mouth, laughed, and said: "It never occurred to me that you would care to do it!"

So soon as he was gone I went to Cambridge, talked with my father who assured me that if Walcott, Shattuck and Fitz felt that it was wise, and I was sure that it was the right thing to do, he should feel satisfied that it was justified, and was in a position to help me to borrow anything that I might need. To his wise moral support I owe everything. In thirty-six hours I was in Baltimore. After a day with Finney I packed my things and within a week found myself in Baltimore as "differentiating physician," with an opportunity to study in the afternoons and evenings.

The year was given largely to studies on the blood. It was a wonderful year for me. What a stimulating group of men it was! Welch, Councilman and Abbott in the laboratory, the Chief and Lafleur in the Medical Department, the Professor and Finney in Surgery, though Finney was then living outside; Kelly and Robb and Ghriskey the most suggestive of men, in the Gynecological staff. My room was next to that of Abbott, who was always moved to song while dress-

ing. I never heard him sing but two songs, "McGinty" and "Annie Roonie." Nuttall came soon, stimulating and delightful; dear old Reese, and Hewetson of blessed memory, and Barker who came before the end of the year. How well I remember the days after Barker's arrival—especially the occasion when Reese and Hewetson, who felt that he should have his hair cut, induced him and me to take a little walk and have a cocktail before dinner. After a long brisk walk they wheeled suddenly into the old Athenaeum Club where Barker found Reese negotiating with the barber to cut his hair. But the barber's scissors were not the scissors of Delilah, for I can never forget the stimulus that he was to all of us.

And the meetings of the old Medical Society held that first year in the library in the main building of the hospital. How vivid they are! One occasion stands out in my memory, an occasion that has not been mentioned so far as I know among the many stories told of the Chief. Old Dr. V. had brought to the Medical Society in a collection of preserve jars and tin basins a common or garden *Taenia saginata* which he suspected to have been the cause of repeated abortions in one of his patients. A delightful old man that he was! The Chief rose with his incomparably graceful and genial manner, and with twinkling eyes said: "When I was in Vienna old Professor Sigmund used to say that lues was the worm that lay at the root of all evil. Although the story is very interesting, I rather think, Dr. V., that in this case it was the other worm." And the old doctor's ample waistcoat trembled as he chuckled gaily.

The year passed like a dream.

The next year I became Resident Physician. It was a great opportunity at first, but I was not altogether satisfied. With all the advantages and the associations of those earlier years, they were, in some ways, rather long years, in which the distracting and time-taking human relations of practice were irksome. After all, to any man with ambition, life, in a certain measure, is a long reaching out to grasp the opportunities afforded by time and leisure to pursue the study of those problems in which he is interested; and the opportunity dangling before him is ever receding.

Little by little, mainly I think through the priceless association with the Chief and with a wonderful body of colleagues and students, but largely through the constant association with human beings, the dignity and the charm of the art of medicine revealed themselves. How hard is the medical art to acquire; how many-sided are its demands; how great are the rewards for him who may begin to approach the proficiency of one like the Chief.

The art of medicine demands certain qualities, attainments and characteristics that no mere learning can supply. Some of these qualities practice itself develops or refines; of some of the desirable attainments the consciousness of one's lack comes mortifyingly back to most of us in the course of our career. The qualities of human sympathy, of patience and equanimity; a general cultivation sufficient to permit the physician to treat with his patient in such fashion that the latter, whatever his station, high or low, may understand him and recognize him as his superior or his peer; the eye and the turn of mind of the naturalist; the power of

accurate observation and quick understanding—it is one thing to observe and another thing to see; an inquiring and questioning spirit which is never satisfied to accept a dogma without proof—a dogma is a human thing—; these are some of the qualities and attainments toward which he who seeks to be a good doctor must strive.

But above all the art of medicine demands practice and experience. One cannot become a good diagnostician without experience. One must have a good basis, one must live, so far as he can, in touch with colleagues who are learned in the various branches of the natural sciences on which the art of diagnosis and therapy calls every day, but that "power to explore" which Hippocrates calls "a large part of the art" can be acquired only through time, by years of intensive experience.

The only essential criticism that I would make of those efforts of recent years with which I have been so sincerely in sympathy, those efforts to place the clinical departments in our schools of medicine on a more solid basis, has been the failure of some to realize that a clinic which is so small as to fail to give the professor of medicine opportunity to utilize fully the best clinicians of his staff, is sadly incomplete. This is a serious defect in a few of the best clinics today. It is a defect, however, that time is quite sure to remedy.

There have always been and there always will be those who, devoting themselves to the intensive study of special problems, seek to substitute, for methods which are fundamental, procedures which in themselves may be great advances and precious acquisitions, but which are complementary and not to be substituted for the old; who seek, as Sergent has well said of certain modern diagnostic procedures, to substitute one sense for another. But one sense may not be substituted for another; the senses are complementary.

There are few short cuts in medicine. All the acquisitions of recent years have not shortened by a day the time that he who would be a skilled clinician must pass by the bedside; other things equal, that experience is still the main essential.

And then there have always been and there always will be those others—the conservative, the prematurely and the naturally old who, subconsciously inferior, dread lest every new refinement or method the significance of which they are unable wholly to comprehend may inevitably lead away from that which seems to them essential. These men are forever trying to protect the world from the fearful ravages of progress. 'Tis a great thing to have a fair modicum of natural contrary-mindedness, but Heaven preserve me from reaching that age at which everything seems to be going to the devil.

That you my dear master and friend, that you who were my companions and students, and are now my teachers, should make my name an excuse for founding this lectureship on a subject that is so dear to me, is an honour far greater than I deserve. That you should seek to perpetuate my name alongside of that of her who was and is the great inspiration of my life, is to do me an honour and to bring me a joy beyond that which I could have conceived—for which I dare not attempt to thank you.

A CONTRIBUTION TO THE STUDY OF MYCOTIC WARTS[1,2]

A. PEÑA CHAVARRIA, M.D., PH.D., AND P. G. SHIPLEY, M.D.

From the Department of Pediatrics, Johns Hopkins University, Baltimore, Maryland

Hyperplastic growths involving the nails of fingers and toes and their adnexa resulting from infection by the higher vegetable organisms are very common in tropical Latin America where they are known under the generic name *Onychomycoses*. This designation is usually incorrect, since involvement of the nail itself is less common than affection of the paronychial tissue and is frequently secondary to it. Usually, the condition is characterized by the presence of wart-like growths of variable size on the *vallum unguis* or on the skin beneath the *margo liber* of the nail. These warts are extremely chronic and under certain conditions are very painful, so that because of their exposed situation and liability to trauma they may prove a serious handicap to the affected individual in the pursuit of his or her daily occupation. Although they are as a rule easily amenable to treatment they may persist, if untreated, for many years. The condition has received relatively little study but several different fungi have been described as invading the nail and the tissues immediately surrounding it. For example, Escomel (1) has reported the presence of a Tricophyton-like fungus in a subungual wart of extreme chronicity.

With the above facts in view we have thought it of interest to report three cases which presented themselves for study in Baltimore during the past year. The patients were all members of one family which had been resident in tropical America for approximately three and a half years.

A. H. Girl, aged 10 years, of American parentage. She had lived for a year and a half in Bluefields, Nicaragua, and previously for two years at Kingston, Jamaica. The child was brought in to be examined for fitness to enter school in this country.

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[1] Received for publication May 16, 1927.

[2] It is a pleasure to express our gratitude and appreciation to Mr. Max Broedel for the drawings with which this paper is illustrated.

Past history and family history. Negative.

There is no complaint of any present illness, except that the child appears pale and may be anemic from residence in the tropics. Physical examination shows a somewhat undernourished, nervous child with patches of erythrasma in the axillae; otherwise quite normal as to laboratory and physical findings. Beneath the nail of the right thumb there is a small warty growth about 3 mm. in diameter, somewhat tender, and slightly reddened, on a base of normal skin. The surface of the growth is mammillated with deep furrows between the papillae.

M. H. Mother of the above patient (A. H.) and a two-year-old baby. No history of lues or tuberculosis in the family.

Past history. M. H., who had lived in the tropics as described above, developed mycotic warts as follows: a lesion on the thumb of 5 months' and a lesion on the middle finger of the same hand (right) of 3 months' duration.

Onset. The lesion on the thumb was first noted as a small blister, with a dark point in the center, which appeared about to break. The areola surrounding it was pale and the blister and the areola were covered with moisture. After a short time the smooth surface of the blister-like area came off, and the lesion appeared rough and wart-like. The area was reddened and the patient thought pus was forming. There was, however, no pyogenic reaction. The lesion was about 0.5 cm. in diameter and was painful, but did not itch. In all probability the infection had been contracted from the daughter whose lesion was of 6 months' standing. After 2 months a nodule appeared on the palmar surface of the terminal phalanx of the middle finger and was evidently due to contact, since the patient was in the habit of making pressure with this finger over the original growth when it was painful.

Macroscopical examination. Small irregularly round area, about 5 mm. in diameter; of a rough, warty aspect, slightly pigmented and broken up into papillae by deep furrows. The wart is surrounded by an areola of smooth, reddened skin. The growth is slightly pigmented on the surface and shows a red color in the depths. It is situated close to the nail on the internal, lateral side of the thumb. The nail, in the region of the growth, is reddened and the surface cannot be polished. Between its edge and the over-hanging matrix, the nail is thin. The base of the lesion is normal skin. The lesion is dry and a great deal of hyperkeratosis is present. Occasionally the papillae fall off or are knocked off, leaving a bleeding and very painful base. There is no metastatic glandular reaction. The growth is painful spontaneously and pain is increased by cold.

B. B. H., the two-year-old baby of the above, developed a lesion on the finger identical with those on the hands of the mother and sister immediately on her return to Nicaragua a few days after being seen in Baltimore.

In the mother's case small pieces of the hyperkeratotic skin over this wart were examined microscopically after treatment with po-

tassium hydroxide solution in the routine fashion. We were unable to find hyphae or spores of any sort in these preparations but here and there were small bodies which appeared radially striated and which in appearance somewhat suggested the organisms from the grains seen on hairs affected with tinea axillaris (nocardia tenuis) after having been subjected to the same procedure. This finding and the clinical appearance of the lesion induced us to make cultures from bits

FIG. 1. THE APPEARANCE OF THE LESIONS ON THE THUMB AND FINGER OF M. H.

of tissue scraped from the wart. We did not feel warranted in removing the growth for histological examination.

Cultures made from the cornified tissue of these warts on Sabouraud's growth-producing medium remained negative except for colonies of staphylococci for a period of twenty days. At the end of this time small hard colonies of a fungus could be detected in the medium. These were fished and subcultured with the following results.

The organism grew much more rapidly on subcultures than in the original tubes, so that visible colonies were obtained in 5 days after

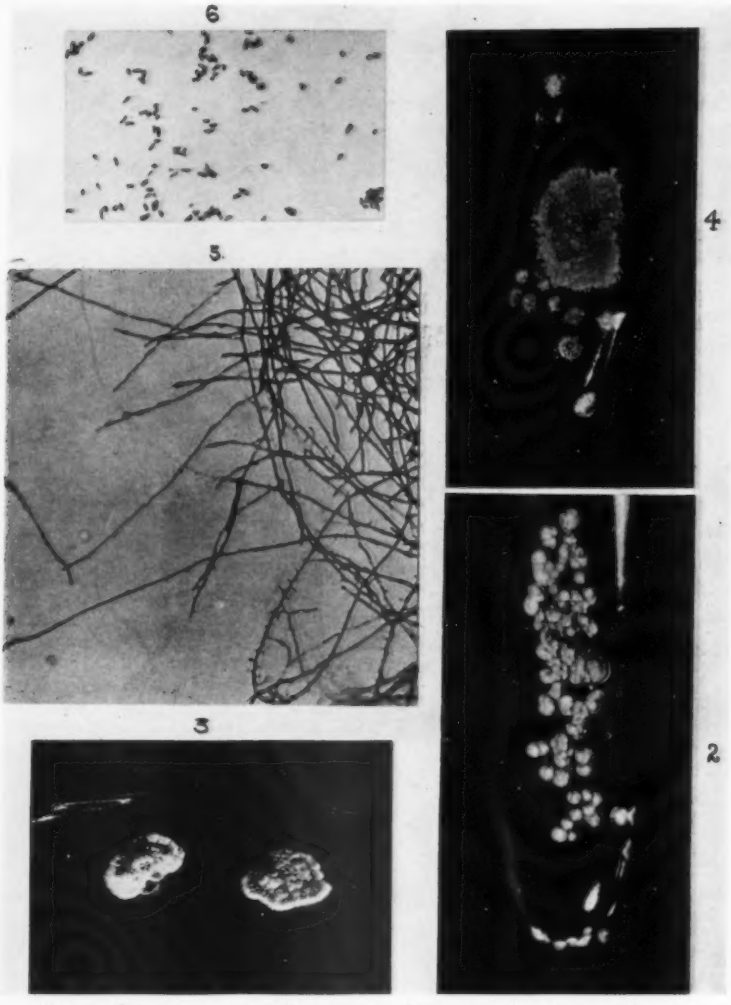

FIG. 2. FIFTEEN-DAY-OLD CULTURE ON SABOURAUD'S MALTOSE SUGAR

FIG. 3. SABOURAUD'S PRESERVATION MEDIUM—15 DAYS OLD

FIG. 4. OLD SPORULATING CULTURE ON PEPTONE AGAR, SHOWING SECONDARY DAUGHTER COLONIES

FIG. 5. MICROPHOTOGRAPH SHOWING CHARACTER OF THE GROWTH AT THE EDGE, A 10-DAY-OLD COLONY

Hanging-drop preparation stained with carbol fuchsin. Branching and beaded hyphae are well shown.

FIG. 6. SHOWING BACILLIFORM CHARACTER OF THE SPORES (CARBOL-FUCHSIN)

subculturing. The organism grew best at a temperature of 22° to 25°C. Growth at 37°C. was very slow and scanty and was abolished in almost all cultures. Growth was obtained under aërobic and partially aërobic conditions but not with complete anaërobiosis.

Sabouraud's (maltose) agar. The organism on this medium grew on and beneath the surface of the agar which was elevated by the sub-surface growth. The young colonies were perfectly white, round, and had a powdery appearance. They soon became covered by a velvety growth of short aerial hyphae, at first snow-white, later of a yellowish-white colour: Colonies 15 to 21 days old were elevated about 1 mm. above the surface of the culture medium and were surrounded by a narrow zone in which the surface of the medium was overgrown by a thin layer of young hyphae. In places the elevated surface of the agar could sometimes be seen through the duvet of aerial hyphae, giving the colony a moist appearance. Old cultures contained a dark brown pigment most of which developed in connection with the sub-surface growth and in the medium itself.

Sabouraud's medium (preservation). Young colonies were round and apparently not elevated above the surface of the medium but the hyphae burrowed into the medium so that, on section, the colonies bore the shape of a kettle-drum. These colonies had a dull powdery effluorescence and were dead white in colour when young. As the cultures grew older they acquired the pale yellow tone of old ivory and took on a coarsely granular appearance, which resulted from the spore formation and the fragmentation of the surface hyphae. The colonies in this stage were often marked by both radial and concentric furrows and were elevated 1 to 1.5 mm. above the surface of the medium. Droplets of water, which became brown after a short time and were filled with spores and fragmenting hyphae, condensed on the surface hyphae. Daughter colonies were formed on the medium by transplantation of the spores which were carried by the water of condensation or through the air in the tube. Old cultures were dull grey in colour like the ash of Cavendish tobacco; they had a very granular appearance and a dark brown stain appeared in the medium about them. Sub-surface growth of hyphae proceeded radially beyond the limits of the surface colony and by transmitted light could be seen through the medium to be concentrically striated in many cul-

tures and to be rayed at the margin. These cultures like all others of this organism had a strong unpleasant odour exactly like that of mouldy old boots.

Vegetable media. No growth could be obtained on potato, beet, banana, carrot or sweet potato.

Broth. No pellicle was formed. The fungus grew at the bottom of the tube and in discrete colonies which floated on the surface or were in contact with the glass or occasionally floated in the medium.

Milk. The organism grew readily and brom-thymol purple showed a transient acid formation after 10 to 14 days. Old cultures (20 to 30 days) became again alkaline and a thin coagulum formed in the milk.

Gelatine and blood serum were liquefied, the former more readily and completely. Growth was luxuriant on serum, the entire medium being covered with a tough, felted membrane after about the fourteenth day of growth. On this medium there was a violet pigment produced, the colour of which was evanescent and changed to dark brown in old cultures (20 to 30 days).

Sugars. No gas or acid was formed in dextrose, lactose, saccharose, maltose, or mannite.

Microscopic and staining characteristics. Growth in pure culture was in the form of a mycelium, the hyphae of which, when properly prepared, or *in vivo*, were 1μ or less in diameter. No distinct nucleus or cell wall could be demonstrated in stained specimens. The individual hyphae were inextricably tangled and twisted about each other, often forming ropes consisting of 3, 4 or even 6 hyphae. Many of the hyphae were wavy. Branching was abundant especially on serum and in broth. Most of the branches were short. The appearance of a colony under the microscope suggested that of a thorn hedge. Only once was any swelling seen at the end of a hypha. Beading of the hyphae was common, especially from cultures grown on broth or serum. The organism was never acid-fast and stained irregularly by Gram's method. In general, the old hyphae retained methyl violet, but the young "growing points" were Gram-negative. Supravital staining of the mycelium with cresyl blue or neutral red showed only an occasional coloured vacuole of small dimensions in the cytoplasm of the fungus.

In old cultures that were sporulating, some of the hyphae would swell and show constrictions at more or less regular intervals which indicated the points of fracture and the separation of the arthrospores. According to the shape of the hyphae (branched, wavy, etc.) and the

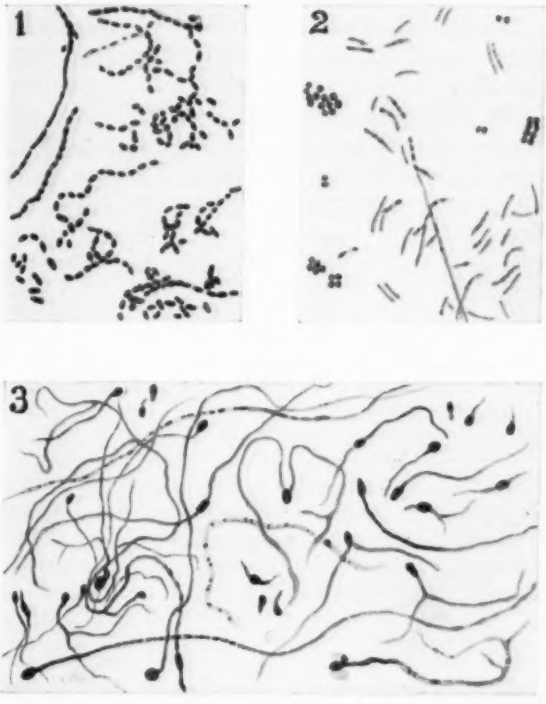

FIG. 7. 1. SPORE-BEARING FRAGMENTS OF HYPHAE FROM A DROPLET OF WATER CONDENSED ON A COLONY (CARBOL-FUCHSIN). 2. ELEMENTS RESEMBLING MYCOBACTERIUM DIPHTHERIAE FROM A TANDEM CULTURE WITH STAPHYLOCOCCI. 3. GERMINATING SPORES

distance between the constrictions the spores might appear bacillus-like, vibrioform, coccoid, Y-shaped or even like coarse spirilla. The arthrospores were highly refractile and were formed within the protoplasm of the hypha which before the release of the spores could be

seen in stained preparations connecting the individual arthrospores to form a chain.

When the organism was grown in tandem in broth with a staphylococcus, the hyphae often broke up into forms which, morphologically, were indistinguishable from the mycobacterium diphtheriae All types of the latter were duplicated in these cultures and the organisms were beaded and barred in the fashion characteristic of the diphtheria bacillus.

Rabbits, rats and guinea-pigs were inoculated, subcutaneously, intracutaneously, intraperitoneally and intratesticularly with suspensions of the mycelium and spores of this organism in sterile water without any pathological result except in the following instance:

Protocol. A male rat weighing 250 grams received 0.1 cc. of a suspension of spores and mycelium into the substance of the left testicle. The animal remained apparently healthy and was sacrificed 40 days later. There were no abnormalities seen at autopsy except that at the site of inoculation a group of the tubules of the testes were greyish white and were sharply outlined against the substance of the normal gland. Sections were made across the testis through this area and stained with haematoxylin and eosin, and with cresyl violet. Examination under the microscope showed these tubules to be necrotic, the tubular cells having become converted into a granular mass in which the tails of the dead spermatozoa were the only distinguishable intact morphological element. There was an hyperplasia and hypertrophy of the interstitial cells in the affected area and some slight increase in the connective-tissue stroma of the gland. The new tissue was very delicate and was infiltrated to a slight degree with mononuclear cells.

Cultures from this testicle were negative, and the fungus could not be identified in the sections. Hence, it is not improbable that the lesion was the result of mechanical injury to the organ at the time of inoculation.

The organism was evidently only very slightly, if at all, pathogenic for lower animals.

There can be no doubt as to the class of organisms to which the one that we have isolated belongs. It is one of the *fungi imperfecti* and belongs, according to Vuillemins' classification to the sub-class Hyphales. This sub-class is divided into four orders, Thallosporales, Hemisporales, Conidiosporales and Microsiphonales, according to the structure of the organism and its method of spore formation. The order Microsiphonales, which includes fungi with fine or bacilliform hyphae and indistinct nuclei, contains two families, the Nocardiaceae

and the Mycobacteriaceae, the former of which includes such microsiphonales as are able to form a mycelium. The genus Nocardia consists of two sections (1) Saprophytica and (2) Parasitica, each subdivided into 3 subsections, Brevis, Minora and Majora. It is not at all clear under which of these subsections our nocardia should be classified, since it shows some of the characteristics of all three.

As we have shown above, this organism is very little if at all pathogenic for rabbits, rats and guinea-pigs, as is very commonly the case for the higher microörganisms. Should, however, this be the causative agent of the lesion we have described, the clinical history of the three patients whom we had the opportunity of examining tells a very different story in regard to human beings. Three members of one family became infected, one from another, and the lesion would seem to have resulted from direct contact with an infected individual rather than indirectly through a vegetable or animal carrier of the microörganism. The possibility of direct transfer or inoculation of the skin from a previously existing lesion without intermediation is clearly shown by the history of the smaller lesion on the middle finger of the second patient in the series since, as we have already stated, this finger was inoculated as a result of pressure made over the older lesion which existed on the thumb of the same hand in an attempt to relieve pain. In all probability the disease, in the first member of this family to be infected, was acquired also by contact with a previously inoculated individual, since there is a history of a close friendship having existed between the family with which this paper deals and a man and wife, members of the American colony in Nicaragua who had been previously resident in the city of Santa Marta in Colombia and who were said to have had very "sore fingers." The nature of this Santa Martan infection is of course not certain, since we could not obtain an accurate clinical description of the condition; it may have been a paronychia of blastomycotic or other origin. Nevertheless, it seems highly probable that this particular strain of nocardia may have been native to Colombia rather than to the country where it was acquired. Indirect transfer of nocardia is a possibility and in fact is not an uncommon occurrence. Such an inoculation usually results from the presence of spores or of the mycelium of the pathogenic agent on thorns or other foreign bodies by which the hands and feet may be

lacerated, and in our experience inoculation with the higher fungi and the resultant formation of cutaneous lesions is very common on the hands and feet of laborers working as cane cutters in the sugar plantations in the tropics.

The lesions were treated successfully with the following ointment.

Acidi salicylici	gr. iii
Hydrargyri chloridi mitis	gr. iv
Adip. lanae	ʒ i

After about 3 weeks the warts dried and fell off and there has been no recurrence of the condition.

The character of the organism and the fact that the family left Baltimore within a few days after examination made immunological studies impossible and re-inoculation experiments on human beings were not done.

REFERENCE

(1) ESCOMEL: Contribution à l'étude de quelques mycoses au Perou. *Bull. de la Soc. de path. exotique*, 1920, t. xiii, p. 663.

THE BACTERICIDAL ACTIVITY OF HEXYLRESORCINOL IN GLYCERINE[1]

With Special Reference to the Influence of Surface Tension in Chemical Disinfection

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THE MECHANISM OF DISINFECTION BY CHEMICAL MEANS

Attempts to interpret biological phenomena in terms of chemical reactivity have led to a number of studies on the influence of various physical factors which might control or influence chemical disinfection. This process, resulting in the death of the organism, is now generally regarded as a chemical reaction between the cell protoplasm and the disinfecting substance.

Among the more fundamental investigations leading to this conclusion are those of Harriette Chick (1), who has presented very convincing evidence that disinfection by chemical means is an orderly time process, exhibiting all of the mathematical characteristics of a chemical reaction of the first order—a so-called unimolecular reaction—such as the hydrolysis of cane sugar. The velocity of such a reaction as well as its completeness is influenced, just as chemical disinfection is influenced, by four physical factors, namely, concentration, temperature, pressure and time.

If, in chemical disinfection, we regard the cell protoplasm as one reagent and the disinfecting substance as the other, it is apparent that a reaction between the two can occur only after the germicide has penetrated the cell membrane of the organism. Under the circumstances, the conditions influencing the reaction might be strictly comparable to those controlling the rate and extent of the reaction which might occur between two reagents separated from one another by a semipermeable membrane. In addition to the physical

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factors mentioned, the velocity and completeness of such a reaction would be largely influenced by factors controlling the rate and the extent of diffusion of one reagent (the germicide) through the membrane (the cell wall) to make contact with the other (protoplasm).

THE INFLUENCE OF SURFACE TENSION IN CHEMICAL DISINFECTION

Billiard and Dieulafe (2) have shown that by lowering the surface tension both osmosis and diffusion are accelerated.

If the foregoing reasoning relative to chemical disinfection is sound, it would be expected that, other conditions being equal, a given disinfectant would be more effective in a solution of low surface tension than in a solution of high surface tension. The rate of diffusion of the germicide through the cell membrane would be increased, within limits, with the reduction in the surface tension of the solvent and consequently the protoplasm of the organism would receive a greater concentration of the germicide within a given time.

There is still another factor which would be expected to increase both the velocity and completeness of this diffusion process in solutions of lowered surface tension, provided the germicide itself is a surface tension reducent. Substances which lower the surface tension of their solvents are mechanically adsorbed on the surfaces of particles, such as bacteria, in suspension in the solution. For this reason it would be expected that a germicide which reduces the surface tension of water in a given concentration, say 1 to 1000, would exist on the surface of the organisms in suspension in that solution, in concentrations actually greater than 1 to 1000. Add to this the increased rate of diffusion of the germicide through the cell membrane which accompanies lowered surface tension, and it becomes clear that not only may the surface tension of germicidal solutions largely determine the effectiveness of definite ranges of dilutions but also that, other things being equal, a germicide which itself lowers the surface tension of water will be more effective than one which does not.

Frobisher (3) has recently presented very convincing experimental evidence in support of these views and cites the work of Berczeller (4), Hansen (5), Billard (6), Liese and Mendel (7), Frobisher (8), Leonard and Frobisher (9), Bechold and Reiner (10) and others as demonstrating that surface tension may play a very important rôle in disinfection by chemical means as well as in other cellular processes.

THE RELATION OF SURFACE TENSION TO THE BACTERICIDAL POWER AND CLINICAL EFFECTIVENESS OF HEXYLRESORCINOL

Working with the acyl and alkyl derivatives of resorcinol, which are all surface tension reducents, Frobisher has demonstrated the existence of a very close relationship between the relative bactericidal power of the compounds in each of these homologous series and their ability to reduce the surface tension of water. Nineteen derivatives were examined. *In both series, the increasing bactericidal power of the successive compounds up to the hexyl and hexylyl derivatives was found to be directly proportional to their increasing power as surface tension reducents.*

Hexylresorcinol is practically as powerful a surface tension reducent as chemically pure sodium oleate (11).

Employing hexylresorcinol on account of its great bactericidal activity (phenol coefficient 72 (12)) in combination with its powerful surface tension reducent properties, Frobisher (3) found that the bactericidal efficiency of a wide range of dilutions could be absolutely controlled merely by manipulating the surface tension of these solutions through the addition of varying amounts of surface tension depressants which are themselves devoid of bactericidal action. The same was found to be true of phenol. In each instance a range of dilutions of the germicide which failed to destroy *Bacillus typhosus* became quickly effective under the same conditions, when the surface tension of the solution was lowered with either sodium oleate or ethyl acetate. He found further that the addition of a certain excess of soap would, in each instance, render inert dilutions of the germicide which would be highly active in the presence of smaller amounts of soap. This was not found to be true of liquid reducents such as ethyl acetate. He advances the explanation that, in the case of sodium oleate, an excess of this soap present in the solution may be adsorbed to the surface of the organism in such a concentration as to be deposited in a solid protective film, thereby preventing the penetration of the germicide through the cell wall. The results of recent experiments by the writers (to be reported in a future communication) suggest that this phenomenon may be observed only within certain limits.

The foregoing discussion of the mechanism of chemical disinfection,

and the important rôle which surface tension may play in this process, deals exclusively with those factors which facilitate the penetration of the germicide into the bacterial cell. Actual contact between the germicide and the cell membrane of the organism is presupposed. The problem of disinfecting any given surface, such as a mucous membrane, presents an additional difficulty, in that the germicidal solution employed must penetrate into microscopic crevices and interstices in order to be brought into actual contact with organisms which may occupy their depths. In this connection it is a well known fact that fluids of low surface tension will seep into the depths of tiny spaces into which fluids of high surface tension will not penetrate. It would appear, then, that germicidal solutions of low surface tension would be more efficient as surface disinfectants than those possessing higher surface tensions. As Frobisher has pointed out, the laws governing capillary rise and certain limitations due to viscosity must be considered in interpreting this generalization. The point it is intended to emphasize in this place is that, other things being equal, a germicide which lowers the surface tension of water will be more efficient than one which does not, first, because such a germicide will be more liable to penetrate microscopic inequalities in surface, and second, because having made contact with the surface of the organism, it not only becomes concentrated on that surface through adsorption but also penetrates the cell membrane of the organism more rapidly.

Abundant clinical evidence in support of this view has been advanced in observations on the treatment of urinary infections with hexylresorcinol (13) (14) (15). In therapeutic doses this drug, which is excreted by the kidney, markedly reduces the surface tension of the urine and under these circumstances imparts active bactericidal properties to it. If the administration of the drug is accompanied by the ingestion of quantities of water or of diuretic drugs, including sodium bicarbonate, citrates, etc., the surface tension of the urine rises sharply and at the same time the urine is found to have been robbed of its bactericidal properties, in spite of the presence of hexylresorcinol. Since hexylresorcinol is equally active in an acid or an alkaline urine, the change in the hydrogen-ion concentration of the urine following either of these procedures bears no relationship to this phenomenon. Also, since none of the drugs employed (sodium

bicarbonate, etc.) will raise the surface tension of a specimen of urine, even when added to it in large amounts, the rise in the surface tension is due not to their presence in the urine but to the diuresis which accompanies their excretion by the kidney.

In this connection it is interesting to note that long before the importance of avoiding diuresis in conjunction with hexylresorcinol therapy was fully understood, Dr. Arthur L. Chute of Boston observed that the drug was very much more effective in patients who were "poor water drinkers" than in those who were successful in carrying out the routine instructions as to increasing the daily fluid intake, ordinarily given to patients with urinary infections (16). On the other hand, those who have failed to avoid diuresis in conjunction with hexylresorcinol in the treatment of urinary infections (17, 18) have experienced the disappointing clinical results which would be confidently predicted on the basis of the foregoing experiments. In the clinical application of hexylresorcinol, the success or failure of the drug to effect complete disinfection of the urinary tract may be reduced in the main to a consideration of surface tension, which in this instance is fortunately very easily controlled.

HEXYLRESORCINOL

As measured by its phenol coefficiency (72) hexylresorcinol is the most powerful phenolic germicide thus far described (19, 20), and its extremely active bactericidal properties appear to be largely dependent upon the surface forces operative in its solutions (3). Owing to its relative lack of toxicity which permits its administration to man in large doses over long periods of time (21), the investigation of its application as an internal antiseptic has delayed an inquiry into its possible advantages as a general antiseptic for use in the disinfection of tissue surfaces, a field which would ordinarily have been investigated first.

An investigation of this nature, which is now in progress, will be reported in detail in future communications. Among the solvents thus far employed in this work 30 per cent glycerine in water appears to be the most efficient. The reasons for this are closely associated with the factor of surface tension and offer striking proof of the accuracy of Frobisher's deductions in attributing to surface forces a

major rôle in the process of disinfection by chemical means. The remainder of this paper is devoted to a description of the experiments which led to this conclusion.

THE ACTIVITY OF HEXYLRESORCINOL IN GLYCERINE

Pure water has a very high surface tension (77 dynes per centimeter) and the surface tension of pure glycerine is not far below it (72.5 dynes per centimeter).

Table I shows the striking difference in the power of hexylresorcinol to reduce the surface tension of these two fluids.[2] Although

TABLE I

Comparison of the power of 1 mgm. of hexylresorcinol per cubic centimeter to reduce the surface tension of pure water and of pure glycerine

FLUID TESTED	SURFACE TENSION IN DYNES* PER CENTIMETER	REDUCTION IN SURFACE TENSION BY HEXYLRESORCINOL
Pure water	77	
Hexylresorcinol 1:1000 in pure water	34	43
Pure glycerine	72.5	
Hexyl-resorcinol 1:1000 in pure glycerine	67	5.5

* One dyne is equivalent to a lifting force of $\frac{1}{981}$ gram.

only slightly soluble in water, 1 mgm. of hexylresorcinol per cubic centimeter reduces the surface tension of this fluid 8 times as powerfully as the same concentration of hexylresorcinol in pure glycerine, in which it is readily soluble.

If, in fact, the bactericidal efficiency of a germicide is enhanced when the surface tension is lowered, as indicated above, hexylresorcinol should be more active in solution in pure water than in pure glycerine, in equivalent concentrations.

Since hexylresorcinol is a very active germicide in solution in both water and glycerine it was necessary, in testing this hypothesis, to select organisms (Gram-negative bacilli) which were known to be

[2] In all of the experiments reported the surface tensiometer of duNouy (22) was employed.

relatively resistant to hexylresorcinol and to reduce the time of exposure to a matter of seconds. The following technic was employed in these and all subsequent experiments:

To 5 cc. of the fluid under examination in a water-bath maintained at 37°C. was added one standard 3 mm. loopful of a 24-hour broth culture of the test organism, which had been transferred daily for at least five days. At intervals of 15, 30 and 60 seconds, one standard 3 mm. loopful was transferred to 10 cc. of broth. As the standard phenol coefficient loop was used, assist-

TABLE II

Difference in velocity of disinfection by 1:1000 hexylresorcinol in pure water and in pure glycerine

	TEST ORGANISM												
	Bacillus pyocyaneus				*Bacillus coli*				*Bacillus typhosus**				
Time of exposure	Control	15 seconds	30 seconds	60 seconds	Control	15 seconds	30 seconds	60 seconds	Control	15 seconds	30 seconds	60 seconds	S.T.†
Hexylresorcinol 1:1000 in pure water	+	0	0	0	+	0	0	0	+	0	0	0	34
Hexylresorcinol 1:1000 in pure glycerine	+	+	+	+	+	+	+	+	+	+	0	0	67

+ = growth; 0 = sterile.

* Hopkins strain.

† Surface tension in dynes per centimeter.

ance in flaming these loops was necessary. All tubes were then incubated for 48 hours at 37.5°C. Standard Witte peptone broth (pH 6.6 to 6.8) was employed throughout.

In working with extremely powerful germicides such as hexylresorcinol, the possibility of transferring to the seeding tube sufficient germicide in the inoculum to prevent the growth of viable organisms must be considered. The control tubes were therefore made up as follows:

To 5 cc. of *the solvent* (without germicide) was added one 3 mm. loopful of the broth culture and the tube agitated. One 3 mm. loopful of this was then transferred to 10 cc. of broth to *which had been added one 3 mm. loopful of the germicidal fluid under examination.* The control tubes therefore received the same inoculum and the same amount of germicide as the seeding tubes.

Table II shows the difference in the velocity of disinfection by 1 to 1000 hexylresorcinol in pure water as compared with the same concentration in pure glycerine. Just as expected, the solution showing the lower surface tension was found to be more quickly effective. On the other hand, a 1 to 400 solution of hexylresorcinol in pure glycerine destroys the three test organisms shown in Table II in 15 seconds, although the surface tension is very little lower than the 1 to 1000 dilution. In other words, the retardation of disinfection which occurs at the higher surface tension ranges may be overcome by increasing the concentration of hexylresorcinol in glycerine.

TABLE III

Effect of the presence of 10 per cent of water in glycerine solution of hexylresorcinol (1:1000)

CONCENTRATION OF GLYCERINE	S.T.† OF THE SOLVENT WITHOUT HEXYLRESORCINOL	S.T.† OF THE SOLUTION WITH 1:1000 HEXYLRESORCINOL	BACTERICIDAL ACTION—B. TYPHOSUS*			
			Control	15 seconds	30 seconds	60 seconds
Pure glycerine	72.5	67	+	+	0	0
10 per cent water in pure glycerine	73	63.5	+	0	0	0

+ = growth; 0 = sterile.

* Hopkins strain.

† Surface tension in dynes per centimeter.

Most organic substances lower the surface tension of water, and dilution of such solutions with water, as would be expected, ordinarily raises the surface tension. The addition of water to glycerine raises the surface tension, *but if hexylresorcinol is present in the glycerine, the addition of water reduces the surface tension and enhances the bactericidal action of the solution.*

The simple experiment recorded in Table III illustrates this phenomenon. The presence of only 10 per cent of water in the 1 to 1000 solution of hexylresorcinol in glycerine *depressed the surface tension 3.5 dynes per centimeter* and enabled the germicide to destroy *Bacillus typhosus* in 15 seconds. In the absence of hexylresorcinol the addition of 10 per cent of water to glycerine *raises the surface tension.*

At this point in the work it became apparent that although glycerine is an ideal solvent for hexylresorcinol a certain amount of water must be present in the solution to free the surface tension re-

ducent properties of the germicide, and thereby enhance its bactericidal activity. The exact composition of the final solution selected for clinical use in surface antisepsis, such as the disinfection of mucous membranes, was therefore determined as that best meeting the following requirements:

1. Lack of irritant properties.
2. Sufficient glycerine present to ensure perfect solution of the hexylresorcinol, not only in the original solution but in all dilutions with water.
3. Sufficient water present with the glycerine to ensure the lowest possible surface tension.
4. Sufficient hexylresorcinol present to ensure very rapid disinfection (15 seconds) not only in the original solution but in those dilutions which might result from its application to moist mucous membranes.

In preliminary experiments a series of solutions of hexylresorcinol varying from 1 to 50 to 1 to 1000 in various concentrations of glycerine in water were studied as to their irritant properties, their bactericidal activity, their surface tensions and the precipitation of the hexylresorcinol on dilution with water.

A one to one thousand solution of hexylresorcinol in aqueous glycerine was finally selected as that concentration which possessed a minimum of irritant action and still destroyed the test organism in 15 seconds.

Having selected 1 to 1000 as the optimal concentration, it remained to be determined just what proportions of glycerine and water should compose the vehicle.

A series of glycerine solutions was then prepared each containing hexylresorcinol 1 to 1000 and various percentages of water from 10 to 90 per cent.

The surface tension of each of these solutions was determined. The curve shown in Fig. 1. which records the drop in the surface tension which accompanied each increase in the percentage of water present, is remarkable both for its regularity and its extent. When it is considered that all of these solutions contained the same amount of hexylresorcinol (1 mgm.) per cubic centimeter, the seemingly anomalous phenomenon of water depressing the surface tension of a glycerine solution some 34 dynes per centimeter is very striking. The explanation, of course, lies in the great difference in the ability of

hexylresorcinol to reduce the surface tension of water as compared with glycerine.

The solution containing 90 per cent of water (S. T. 33) was cloudy and that containing 80 per cent of water (S. T. 34.3) was faintly

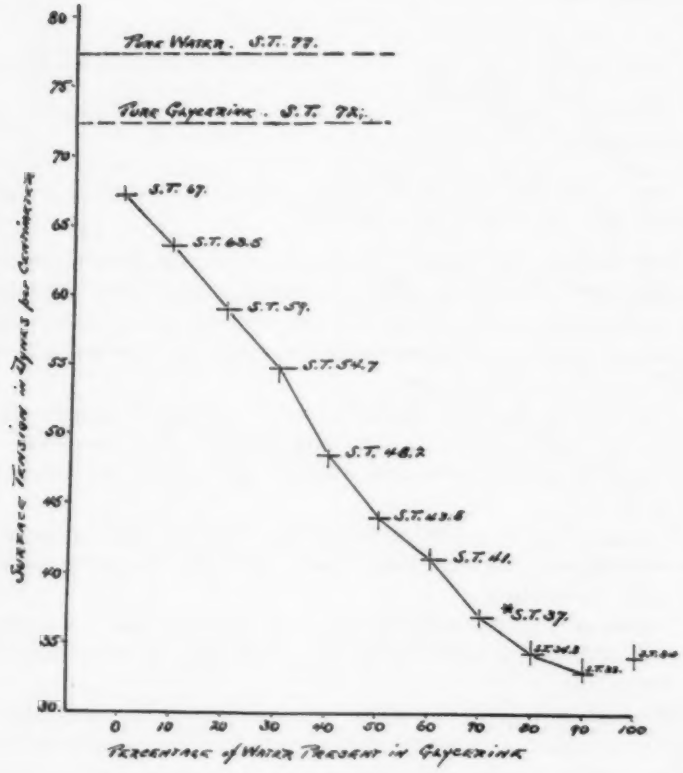

FIG. 1

* Solution S. T. 37: Optimum. See text.

opalescent. The solution containing 70 per cent of water and 30 per cent of glycerine (S. T. 37) was clear, and remained clear on dilution with water in all proportions. Since this solution showed the lowest

surface tension of those in which the hexylresorcinol remained in perfect solution, and since its irritant properties were found to be so mild as to permit its use on sensitive mucous membranes, it was selected for more detailed examination of its bactericidal activity.

This solution consisting of 30 per cent of glycerine and 70 per cent of water in which is dissolved 1 mgm. of hexylresorcinol per cubic centimeter and which possesses a surface tension of 37 dynes per centimeter,

TABLE IV

Bactericidal activity of hexylresorcinol in Solution S. T. 37

TEST ORGANISMS	CONTROL	15 SECONDS	30 SECONDS	60 SECONDS	CULTURE MEDIA
Bacillus coli	+	0	0	0	Witte peptone broth*
Bacillus typhosus	+	0	0	0	Witte peptone broth
Bacillus pyocyaneus	+	0	0	0	Witte peptone broth
Bacillus proteus	+	0	0	0	Witte peptone broth
Staphylococcus albus	+	0	0	0	Witte peptone broth
Staphylococcus aureus	+	0	0	0	Witte peptone broth
Bacillus diphtheriae	+	0	0	0	Beef infusion broth
Bacillus hofmanni	+	0	0	0	Beef infusion broth
Streptococcus hemolyticus	+	0	0	0	Beef infusion broth
Streptococcus viridans	+	0	0	0	Beef infusion broth
Pneumococcus Type I	+	0	0	0	Beef infusion broth
Pneumococcus Type IV	+	0	0	0	Beef infusion broth
Micrococcus meningitidis	+	0	0	0	Beef infusion broth
Micrococcus gonorrhœæ	+	0	0	0	Brain infusion broth
Spirillum metchnikovi	+	0	0	0	Witte peptone broth

+ = growth; 0 = sterile.

* American Public Health Association standard (23) (pH 6.6 to 6.8).

is designated, as a matter of convenience, as "Solution S. T. 37" (See Fig. 1).

Table IV shows the activity of Solution S. T. 37 against a fairly comprehensive list of pathogenic microorganisms. All were destroyed in 15 seconds.

The technic employed in these tests was precisely that described above except for the media used as indicated in Table IV.

Such organisms as *Endamoeba coli* and *Iodamoeba williamsi*; spirochaetes, such as *Leptospira icterohemorrhagiae* and various flagellates,

such as *Trypanosoma lewisi* and *Trichomonas hominis*,[3] are instantly destroyed and disappear completely on contact with Solution S. T. 37.

TABLE V

Bactericidal activity of hexylresorcinol in various dilutions of Solution S. T. 37

DILUTIONS OF S. T. 37 WITH DISTILLED WATER	S.T.†	BACILLUS TYPHOSUS*						STAPHYLOCOCCUS AUREUS‡					
		Control	15 seconds	30 seconds	60 seconds	2 minutes	5 minutes	Control	15 seconds	30 seconds	60 seconds	2 minutes	5 minutes
Diluted with 1 part water	39.6	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 2 parts water	43.0	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 3 parts water	45.7	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 4 parts water	47.0	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 5 parts water	49.0	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 6 parts water	50.4	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 7 parts water	51.1	+	0	0	0	0	0	+	0	0	0	0	0
Diluted with 8 parts water	51.1	+	0	0	0	0	0	+	+	0	0	0	0
Diluted with 9 parts water	53.1	+	0	0	0	0	0	+	+	+	0	0	0

+ = growth; 0 = sterile.

* Hopkins strain.

† Surface tension in dynes per centimeter.

‡ This strain previously described (24).

TABLE VI

Bactericidal activity of various dilutions of Solutions S. T. 37 in the presence of organic matter

DILUTIONS OF S.T. 37 WITH DISTILLED WATER 2 PER CENT PEPTONE AND 1 PER CENT GELATINE ADDED	BACILLUS TYPHOSUS*				STAPHLOCOCCUS AUREUS*			
	Control	15 seconds	30 seconds	60 seconds	Control	15 seconds	30 seconds	60 seconds
Undiluted	+	0	0	0	+	0	0	0
Diluted with 1 part water	+	0	0	0	+	0	0	0
Diluted with 2 parts water	+	0	0	0	+	0	0	0
Diluted with 3 parts water	+	0	0	0	+	0	0	0

+ = growth; 0 = sterile.

* See footnote to Table V.

Since any germicidal solution must suffer at least some dilution on being applied to a moist mucous surface and may sometimes suffer

[3] We are indebted to Dr. L. B. Lange and to Mr. Conrad Bauer for this material.

very considerable dilution, as when introduced into the pelvis of an actively functioning kidney, a range of dilutions of Solution S. T. 37 sure to cover those likely to be encountered under clinical conditions was next examined as to the velocity of their bactericidal action. The technic employed was precisely that described above. It is apparent from the results shown in Table V that Solution S. T. 37 retains its rapid bactericidal action within a range of dilutions much greater than those which are at all likely to be met with clinically.

All bactericidal substances suffer at least some reduction in their activity when brought in contact with organic matter. Since, under clinical conditions, organic matter such as mucus, cellular debris, etc. is always present, the activity of those dilutions of Solution S. T. 37 most likely to approximate the conditions of practical application was tested in the presence of a standard organic mixture. This organic mixture consisted of 2 per cent peptone and 1 per cent gelatine. The dilutions of Solution S. T. 37 with water were first made up and the requisite amount of peptone and gelatine then weighed out and added in substance. In each instance a small portion of the gelatin failed to enter into solution. The technic employed in these tests was precisely that described above. The results are shown in Table VI. It appears from this experiment that the presence of a standard organic mixture does not retard the bactericidal action of Solution S. T. 37 in these dilutions.

Stability. Aqueous solutions of hexylresorcinol suffer no deterioration in bactericidal activity even after many months at room temperature. Solution S. T. 37 still destroys *B. typhosus* and *Staph. aureus* in 15 seconds after six weeks' standing at room temperature. Further observations on stability will be reported in future communications together with clinical results in the application of this solution.

CONCLUSIONS

1. Surface forces play a major rôle in disinfection by chemical means.

2. Under equivalent conditions, a germicide which depresses the surface tension of water is more efficient than one which does not for the following reasons:

a. Due to the greater extensibility of the fluid film of low surface

tension the germicidal solution is more liable to penetrate microscopic inequalities in surface, inaccessible to fluids of high surface tension.

b. Germicides which reduce surface tension are adsorbed by particles in suspension, such as bacteria. The germicide concentrates at the most effective point, *i.e.*, on the surface of the organism.

c. Diffusion of the germicide through the cell membrane of the organism is accelerated as the surface tension is lowered.

3. Hexylresorcinol, in aqueous solution, is a powerful surface tension reducent. It is readily soluble in glycerine. Its bactericidal activity in solutions containing various proportions of glycerine and water is inversely proportional to the surface tension of those solutions, *i.e.*, the lower the surface tension, the greater is their bactericidal activity.

4. A solution containing 30 per cent glycerine and 70 per cent water in which is dissolved 1 mgm. of hexylresorcinol per cubic centimeter (1 to 1000) possesses a surface tension of 37 dynes per centimeter (Solution S. T. 37) and appears to represent the optimal composition for clinical application in tissue surface disinfection, for the following reasons:

a. It is non-toxic and non-irritating.

b. The hexylresorcinol is held in perfect solution in all dilutions.

c. The surface tension is very low.

d. All the major types of pathogenic microörganisms are destroyed in less than 15 seconds on contact with this solution.

e. Its bactericidal activity is retained (15-second standard) under all conditions of dilution likely to be encountered in clinical application as well as in the presence of organic matter.

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HEART LESIONS PRODUCED BY THE DEEP X-RAY

An Experimental and Clinical Study[1,2]

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For a long time muscle and particularly heart muscle was considered relatively insensitive to the action of Roentgen ray, being classed with cartilage and bone among the most resistant tissues of the body. Beeck and Hirsch (1), however, in 1916, suggested the possibility of actual damage to the heart muscle during therapeutic irradiation. They felt, however, that the changes were not specific and that the brown atrophy and simple atrophy observed in these irradiated parts were seen also in many other conditions.

Kotzenberg and Kautz (2), in 1919, reporting upon the treatment of cardiac asthma and angina pectoris with x-ray, emphasized the resistance of the heart so far as any deleterious effects were concerned, but they made no anatomical or histological studies.

During 1924 two important studies appeared on the subject. The one by Davis (3), an experimental observation, dealt principally with the chronic lung changes, but gross and microscopic changes in the heart were also recorded. These changes Davis summarized as follows: "Cardiac changes were observed in all but two dogs. These changes consisted in marked increase in the thickness of the wall of the right auricle which also appeared to be the seat of numerous petechial hemorrhages. Microscopically, the right anterior auricular wall showed numerous areas of cell necrosis, proliferation of connective tissue, extravasation of red blood corpuscles and necrotic muscle fibers fused into hyaline masses."

The second communication in 1924 was that by Schweizer (4). He described a case of Hodgkin's disease in which the patient had

[1] Read before the American Society of Experimental Pathologists, April, 1927 and the American Climatological and Clinical Association May, 1927.

[2] Received for publication May 28, 1927.

been given deep irradiation over the chest. The gross changes were not striking, but microscopically there was marked atrophy of the muscle fibers and granular degeneration. Some muscle fibers in the later stages appeared as dilated empty tubes. The interstitial tissue showed a marked vacuolar degeneration and the capillaries a much thickened wall which was richly nucleated.

In 1925, Smith and others (5) recommended the treatment of pertussis with the Roentgen ray, laying emphasis on an attempt to reduce the lymph gland enlargement about the hilus of the lungs. This treatment was very light, since they made use of only 60 kilovolts and 1 mm. of aluminum as a filter, with a tube distance of 28 inches, so that it seems unlikely that it could have had any effect on the heart. But if the opportunity presents itself, microscopical sections from hearts of patients so treated should be studied for changes similar to those reported in experimental animals.

Levy and Golden (6) in 1925 advocated deep x-ray as a therapeutic agent for the treatment of rheumatic endocarditis. Here also the treatment was very light, consisting of only one-tenth of an erythema dose, and could hardly be expected to produce any marked effect on the myocardium.

The work presented here is a continuation of the studies upon the chronic effects on the tissues which may be produced with the deep x-ray.

In a series of eight animals deep x-ray was applied high over the liver in an area which included most of the anterior thoracic wall. Care was taken in this group to protect only the stomach and abdominal viscera. In the observation of these animals the liver deficiency was of minor importance but cardiac symptoms, manifested by labored breathing, cyanosis and irregularity of the heart along with anatomical changes, led us to apply the x-ray directly over the heart and to observe more closely all the cardio-vascular manifestations including electrocardiographic tracings.

METHODS

Irradiation was given with the modern water-cooled tube delivering 200 kilovolts, 30 milliamperes at 50 cm. skin distance, a filter of 1 mm. of copper and 1 mm. of aluminum being employed. This set-up

was always used. The dosage is referred to in minutes throughout this communication. An exposure of 15 minutes represents approximately one human erythema dose. During the administration of the x-ray the animal was kept in position by means of a specially constructed holder, the sides of which were adjustable. The electrocardiographic hook-up was made in the usual way and the use of sedatives or anaesthetics was avoided.

EXPERIMENTAL

The data to be presented here may be grouped about three series of animals:

1. Including 13 dogs and 5 sheep irradiated over the anterior thoracic wall through an area 7 × 9 cm. and 10 × 12 cm., respectively.

2. A group of 8 dogs treated through a large area, 15 × 15 cm., covering almost the entire anterior thoracic wall including the liver area, care being taken to protect only the stomach and intestines.

3. A group of animals, 3 in number, exposed through the right chest wall, with a window 7 × 9 cm.

In the first series the experiments may be divided into those in which the animals survived only about 30 days and those which survived for three months or more. Of the animals which survived only 30 days, 5 were sheep and 3 were dogs. Over the area of irradiation there was usually loss of hair and less frequently ulceration. Dosage for the sheep ranged from 120 to 280 minutes. Dosage for the dogs that lived 30 days or less ranged from 75 to 280 minutes. With the larger dosage the smaller area of application was used. After the course of irradiation was started, some of the animals, both dogs and sheep, were much quieter and tended to lie around in the cages a great deal. They ate well, however, and for the most part remained in a good state of nutrition. The sheep apparently all succumbed as a direct result of the x-ray treatment, while the dogs died from other causes. At autopsy the thoracic wall in the area of irradiation showed the tissues oedematous and congested. The skin particularly was very thick and tough. The abdominal organs were constantly found congested but of the usual size. In the thorax there was no pleural effusion. The lungs in the case of the sheep were voluminous, especially the lower lobes, and the pleura was marked here and there with gray

patches of thickening. On section through the lungs, the lower lobes were found to be almost solid and a large amount of thin foamy fluid was squeezed out.

The pericardial sac was dilated regularly and filled with fluid ranging from 80 to 150 cc. in all the sheep. The pericardium, however, was everywhere smooth and glistening. The heart was

FIG. 1. (SHEEP NO. 3.) PHOTOMICROGRAPH, 4 MM. OBJECTIVE, SHEEP'S HEART. SHOWING VACUOLAR AND HYALINE DEGENERATION WITH INDISTINCT STRIATIONS AND OEDEMA OF THE CONNECTIVE TISSUE

greatly distended, being from two to three times the normal size. The dilatation was confined for the most part to the right auricle and the right ventricle. In the wall of the right ventricle, the interventricular septum, and the wall of the left ventricle, the microscopic changes in the muscle are similar, that is, the fibers are swollen and the striations are quite indistinct, giving to the whole fiber a velvety fuzzy appearance. Between the fibers are seen engorged capillaries with occasional extravasations of blood and with some round and wandering cell infiltration. The muscle does not stain uniformly. In places patches take the stain more lightly than in others. In these lightly

staining patches striations are indistinct (Fig. 1). In the case of one of the sheep receiving 240 minutes of x-ray over a period of 30 days there is, in addition to the changes noted in the muscle, an intense polymorphonuclear infiltration. The sheep were included in this group particularly in order that the conduction system might be studied more readily. Microscopically, the larger and smaller

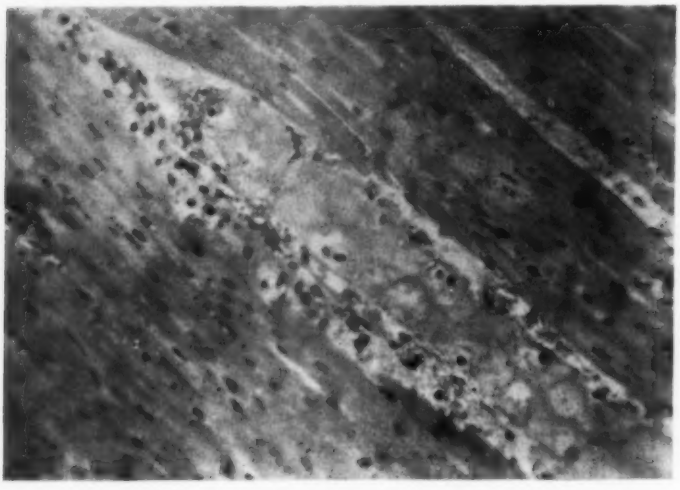

FIG. 2. (SHEEP NO. 3.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, SHOWING BUNDLE BRANCH IN ACUTE 30-DAY STAGE—SHEEP'S HEART

The cells of the bundle are vacuolated and poorly staining. Bundle is surrounded by oedematous connective tissue which is infiltrated by round, wandering cells and polymorphonuclear leucocytes. The adjacent muscle fibers have lost their striations for the most part, appearing fuzzy throughout. There is much congestion and extravasation between the muscle fibers.

branches of the auriculo-ventricular bundle are well preserved when compared with the damage to the muscle proper. The larger branches show only thinning of the fibrils at the margin of the cells with vacuolation and distortion of the nuclei, while some of the smaller branches, which lie in areas where the muscle stains poorly and is infiltrated by leucocytes, show the individual cells distorted, vacuolated, poorly

staining and with shriveled nuclei. The infiltration, however, does not extend into the branches of the bundle and in no case was hemorrhage or complete destruction of the bundle found (Figs. 2 and 3).

The animals rayed directly over the anterior thoracic wall and which lived for more than 30 days (all were dogs), numbered four in all. These animals received from 130 to 155 minutes of irradiation

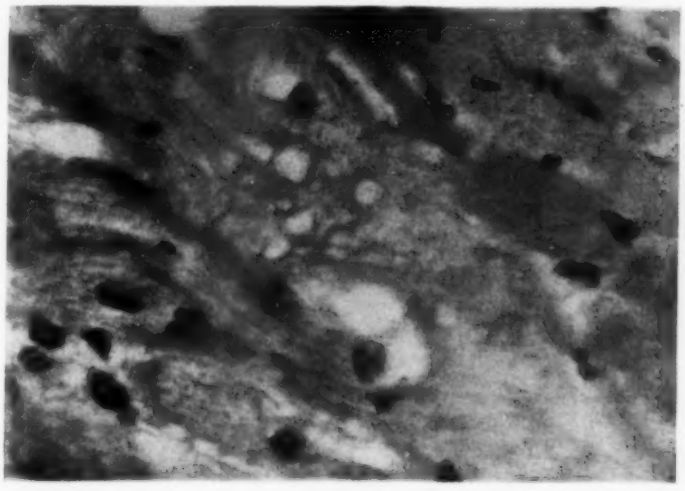

FIG. 3. PHOTOMICROGRAPH, 4 MM. OBJECTIVE, TAKEN THROUGH SMALL BUNDLE BRANCH AND MUSCLE

The bundle is distorted and hardly recognizable. The muscle fibers do not show striations plainly but give a fuzzy frayed appearance. There is also round and polymorphonuclear infiltration. (Sheep no. 3.)

over periods ranging from 3 to 5 months. They remained in as good condition as the first part of the group except that in the later stages deep ulceration occurred in two animals and cachexia set in. At autopsy the findings, except for the heart, were similar to those described in animals dying more acutely. In the heart there was more dilatation and more congestion of the superficial vessels. The right auricle in all cases was involved in a hemorrhagic process of greater or less extent, resembling that described by Davis. In some cases this

involved only the tip of the auricular appendage. In others it involved the entire auricular wall and extended through the sulcus terminalis at the base of the superior vena cava (Fig. 4). When the heart was opened this infiltration of the auricle was seen to extend through to the endocardium. The latter was reddish-yellow in color as a result of the infiltration. In some instances the tip of the appendage was thrombosed. The thickness of the auricular wall of these

FIG. 4. (DOG K 71.) GROSS APPEARANCE OF HEART SHOWING EXTENSIVE HEMORRHAGE OF THE RIGHT AURICLE AND ENGORGEMENT OF SUPERFICIAL BLOOD VESSELS THROUGHOUT

The right ventricle is greatly dilated and the left to a lesser extent.

animals ranged from 3 to 4 mm. On cut section the surface was mottled gray and red. In two of the animals the hemorrhagic infiltration extended around the pulmonary artery and over some of the adjacent fatty tissue. The valves were intact throughout. The ventricular walls were thinned out on the right side, averaging from 2 to 4 mm., and on the left side from 5 to 9 mm., depending upon the degree of dilatation. The cut surface of the ventricular walls was

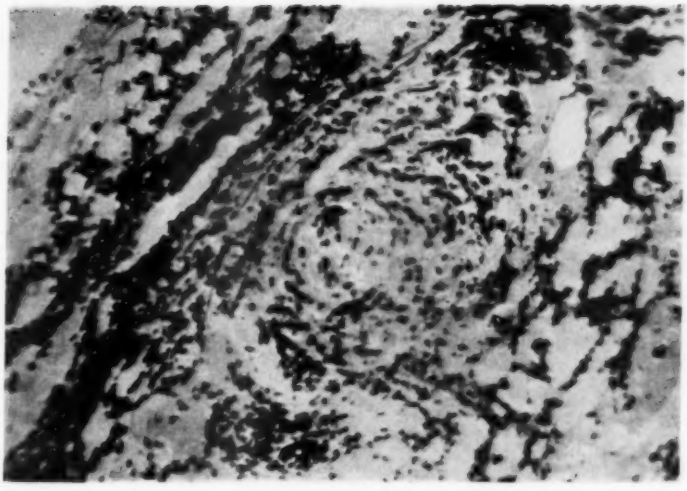

FIG. 5. (DOG H 72.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, SHOWING SMALL ARTERIOLE IN THE WALL OF THE PULMONARY ARTERY COMPLETELY OBLITERATED AND THE SURROUNDING TISSUE OEDEMATOUS AND HEMORRHAGIC

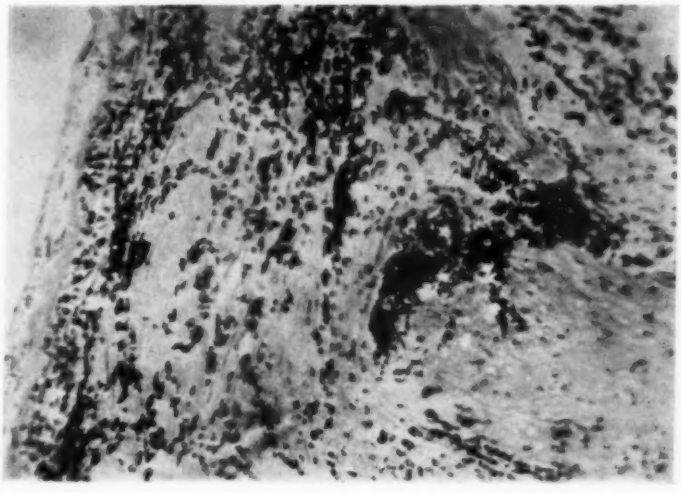

FIG. 6. (DOG K 71.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, SHOWING WALL OF RIGHT AURICLE WITH EXTENSIVE HYALINE DEGENERATION AND HEMORRHAGE

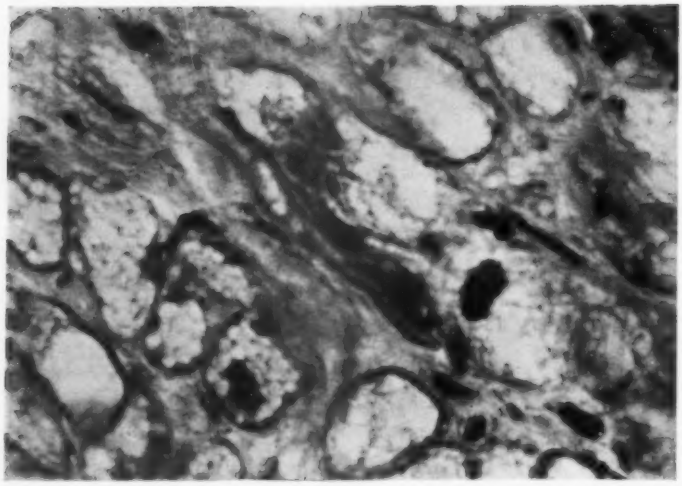

FIG. 7. (DOG G 75.) PHOTOMICROGRAPH, 4 MM. OBJECTIVE, SHOWING MUSCLE FIBERS CUT IN CROSS-SECTION

The cytoplasm is vacuolar throughout and the nuclei are irregular.

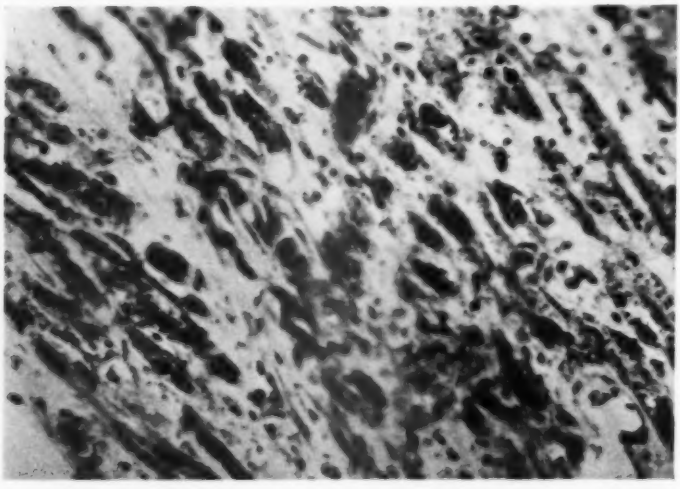

FIG. 8. (DOG H 72.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, FROM WALL OF RIGHT AURICLE STAINED WITH SUDAN III

The individual fibers are heavily infiltrated with fat.

dark reddish-brown in color but no hemorrhages were found. *Microscopically*, a section through the distal portion of the auricular wall shows the muscle tissue largely replaced by areas of homogeneous, pink-staining, hyaline degeneration. About these areas there is intensive hemorrhagic infiltration throughout the wall. The blood vessels are thick-walled and in some cases obliterated (Figs. 5, 6). The few remaining muscle fibers in the auricular wall stain very lightly

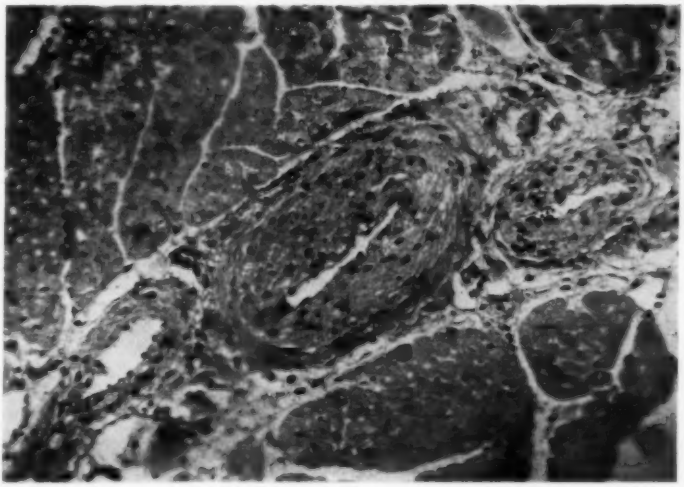

FIG. 9. (DOG H 72.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, INCLUDING BRANCHES OF RIGHT CORONARY ARTERY

The walls are much thicker than usual and richly nucleated while the lumina are much narrowed.

and striations are difficult to make out. Still other fibers are seen only as tubular structures filled with vacuoles. The nuclei in these degenerated fibers are irregular and pyknotic. The degeneration in the fibers is unusually well seen in those which are cut in cross-section. Here the sarcolemma appears as a distinct dark-staining membrane and the substance of the cells is made up of large vacuoles. These cells cut in cross-section are not unlike xanthoma cells when seen in

frozen sections (Fig. 7). Fat stains show the individual fibers infiltrated throughout with smaller and larger fat globules (Fig. 8).

From three hearts taken from animals in this group serial sections were made through the sulcus terminalis in an attempt to identify

FIG. 10. (DOG B 77.) SECTION THROUGH HEART AFTER IRRADIATION FROM RIGHT SIDE SHOWING HYALINE DEGENERATION AND HEMORRHAGE IN THE LOWER PART OF THE RIGHT VENTRICULAR WALL AND THE TIP OF THE LEFT VENTRICLE; ALSO DISCOLORATION OF THE MUSCLE IN THE INTRAVENTRICULAR SEPTUM

The right auricle shows only dilatation.

tissue of the sinoauricular node. The degenerative process, however, was so extensive that none of the nodal structures were discernible.

Sections taken from the right ventricular wall, the interventricular septum and the left ventricle show no hemorrhage or hyaline degeneration. Here there is atrophy of the individual muscle fibers which

appear as slender tubes separated by spaces almost as wide as the fibers themselves. Many of the fibers show the striations poorly, the cytoplasm being made up of fine granules or larger vacuoles surrounded by the darker-staining sarcolemma. In some places the fibers are so damaged that they show no normal structures, but appear as homogeneous, pink-staining, hyaline masses. The interstitial tissue is very abundant and is often finely granular or vacuolated; it is particularly abundant about the smaller blood vessels and may be infiltrated by round and wandering cells. The blood vessels themselves have thick walls and narrow lumina (Fig. 9).

The second group of animals—those treated over a larger area including the liver—show more fibrosis of the lung and liver but in the heart itself changes identical with those described in the second part of the first series.

In the third group only one animal has come to autopsy. It received a total of 190 minutes during a period of 4 months. This had resulted in loss of hair and superficial ulceration in the axillary fold of the skin. This animal weighed 25 kilos and remained fairly active and in good nutrition throughout but showed cyanosis after exertion. On the morning of his death he was seen walking about the cage and eating, but shortly after was found stretched out on the floor dead—the end having come apparently without noise or struggle.

On section the abdominal organs and kidneys were deeply congested. The pleural cavities showed no excess of fluid but the right lung showed areas of thickened pleura and fibrosis. The pericardial sac contained 120 cc. of clear yellowish fluid, but the pericardial surfaces were smooth. The heart weighed 139 grams. The lower half of the right ventricle and the tip of the left ventricle were roughened and grayish-red in color. The auricles were dark grayish-red in color but showed no thickening or hemorrhage. When the heart was opened, the ventricular walls were mottled gray and reddish-brown in the area corresponding to the roughened epicardium. The intraventricular septum was softened and grayish-red as contrasted with the light red of the less damaged muscle (Fig. 10).

Microscopically, these areas show thickening and hyaline degeneration of the epicardium and hemorrhage, with atrophy and granular and vacuolar degeneration of the muscle fibers. Sections from the

right auricle show degeneration and atrophy of the muscle fibers without hemorrhage.

HUMAN CASE REPORTS

In going back over our records of the patients with malignant disease of the mediastinum who had received considerable amounts of x-ray treatment and later came to autopsy, we found three in which microscopic examination of the myocardium yielded interesting changes which we felt were quite similar to those observed in our dogs that had been exposed to deep x-ray.

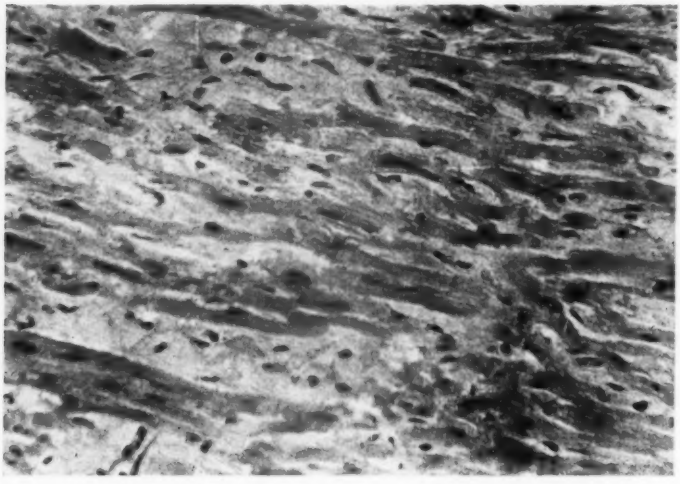

FIG. 11. (HUMAN CASE NO. 1.) 16 MM. OBJECTIVE SHOWING ATROPHY OF MUSCLE FIBERS, FRAGMENTATION AND DEGENERATION OF SOME

Case No. 1 (Hospital No. 53895). A woman, aged 36 years, was found to have lymphosarcoma, as proven by biopsy of a cervical lymph node. X-ray plates of the chest showed a rather massive involvement of the mediastinal region extending out into the right lung. She had two series of deep x-ray treatment, the first over a period of 3 or 4 days in January, 1925, the areas exposed being the anterior portion of the chest, the posterior and right side of the chest and the right axilla, totaling 70 minutes. The second series of treatments was given in March, 1925, over similar areas, totaling 76 minutes. The patient died on September 27, 1925.

Autopsy showed an empyema on the right which had been drained by operation. The right lung was collapsed and airless and the upper lobes were transformed into a whitish-gray tumor mass, the center of which was cavitated and contained blackish necrotic debris. There were a few small tumor masses in the left lung. The pericardial sac contained 20 cc. of clear straw-colored fluid; the surfaces were smooth and glistening. The epicardium was smooth and the subepicardial fat was oedematous. In the wall of the left auricle there was a tumor nodule, 2 cm. in diameter. On section the valves were intact and the endocardium was smooth. The myocardium was soft and dark reddish-brown in color. *Microscopically*,

FIG. 12. (HUMAN CASE NO. 2.) 16 MM. OBJECTIVE SHOWING ATROPHY OF MUSCLE FIBERS AND FRAYED FUZZY APPEARANCE SUCH AS SEEN IN THE ACUTE STAGE OF THE EXPERIMENTAL ANIMAL

the heart muscle fibers are narrow and atrophic. The striations show well but most of the cells present marked brown pigmentation. The interstitial tissue is abundant and vacuolated. Only in scattered areas is granular, vacuolar or hyaline degeneration of the fibers proper seen (Fig. 11).

Case No. 2 (*Hospital No. 60833*). A merchant, aged 62 years, who complained of asthma of two years' duration, was admitted to the hospital June 3, 1925. Physical and x-ray examination gave evidence of a mediastinal tumor with extension into the hilum of the left lung. On June 9 he was given 15 minutes of x-ray anteriorly over the mediastinum. On June 10 the mediastinum was treated pos-

teriorly for 30 minutes, 15 minutes from a right and 15 minutes from a left angle, a total of 45 minutes of x-ray in two days. Death occurred on August 3, 1925.

Autopsy showed primary carcinoma of the pancreas with metastasis to the mediastinal, retroperitoneal and bronchial lymph nodes and left lung. *Grossly*, the heart was of the size of the right fist. The endocardium was smooth and there was much subepicardial fat. On section the valves were intact. The myocardium was pale, soft and flabby. *Microscopically*, the heart muscle fibers are of the usual size but they have a frayed fuzzy appearance and the striations are indis-

FIG. 13. (HUMAN CASE NO. 3.) PHOTOMICROGRAPH, 16 MM. OBJECTIVE, TAKEN FROM VENTRICLE; SHOWS ATROPHY OF MUSCLE FIBERS WITH GRANULAR, VACUOLAR AND HYALINE DEGENERATION OF SOME

Small blood vessel shows much thickened hyalinized walls and a narrow lumen. It is surrounded by an excess of lightly staining vacuolated connective tissue.

tinct. There is marked brown pigmentation about the nuclei. The fibers are separated by an excess of interstitial tissue which shows vacuolation with round and wandering cell infiltration (Fig. 12).

Case No. 3 (Hospital No. 60348). A woman, aged 23 years, was found in May, 1925 to have lymphosarcoma, as proven by biopsy of a cervical lymph gland. She was observed for a period of over one and one-half years, and during this time there were several hospital admissions. The pulse rate averaged from 100 to 120 after the first x-ray treatment. X-rays of the chest showed a nodular enlarge-

ment of the mediastinal shadow extending outward somewhat into the lung fields. She was given the following x-ray treatments:

On June 1, 1925, she was given x-ray treatment over the chest anteriorly, posteriorly and through the axillae for a total of 64 minutes; on August 5, 1925, in a similar way, for 26 minutes; on September 28, 1925, for 65 minutes; and on September 1, 1926, for 42 minutes; a total of 197 minutes. Death occurred on December 18, 1926.

At *autopsy* there was an acute fibrinous pleurisy on the right with erysipelas involving the back, sides, neck and chest. Both lungs in the lower lobes showed numerous tumor nodules that extended well into the parenchyma, and a tumor mass was present in the mediastinum surrounding the larynx. A second nodule was attached to the mediastinum and to the pericardial sac. The pericardial sac contained 20 cc. of clear straw-colored fluid and the surfaces were smooth and glistening. The undissected heart weighed 320 grams. On section, the valves and endocardium appeared normal. The myocardium was dark red in color and of good consistence. The wall of the ventricle was 1.5 cm. in thickness. *Microscopically*, the changes are those seen and described as occurring in the ventricles of the dogs living from 3 to 4 months after irradiation over the heart. The auricles show no hemorrhages or hyaline degeneration. The sections from various areas show marked atrophy of the fibers and a corresponding increase in the amount of interstitial tissue. Of many fibers the sarcolemma and vacuolated cytoplasm are all that remain. Still others have undergone complete hyaline degeneration. The small arterioles are thick-walled and surrounded by an excess of fibrous tissue (Fig. 13).

ELECTROCARDIOGRAPHIC STUDIES

Previous experiments on the heart intended to produce abnormal changes in the electrocardiogram have generally been limited to operative measures under general anaesthesia, while the intact heart was beating *in situ*. The means used for producing abnormal changes have varied from crushing or burning, excising or ligating certain portions of the heart or exposing the myocardium in various locations to electrical stimuli of different characters; or observations have been made upon the effect on the heart of the injection of certain substances into the blood stream or into portions of the organ itself. Generally, at the end of such an experiment it has been necessary to sacrifice the animal.

Essentially chronic and diffuse myocardial changes comparable to those found in the human being have been difficult to produce with any uniformity. Hamburger (7) and his associates approached the condition by a series of experiments in which they injected lycopodium

spores into the coronary arteries of dogs. In the myocardial damage resulting from the experimental use of deep x-ray as here reported, lesions have been produced which are characterized by rather diffuse destruction of the myocardium in the acute stages, followed later on by fibrosis and by narrowing of small vessels. These changes, especially those of the more chronic type, may be likened in character to some of the degenerative myocardial lesions found in man.

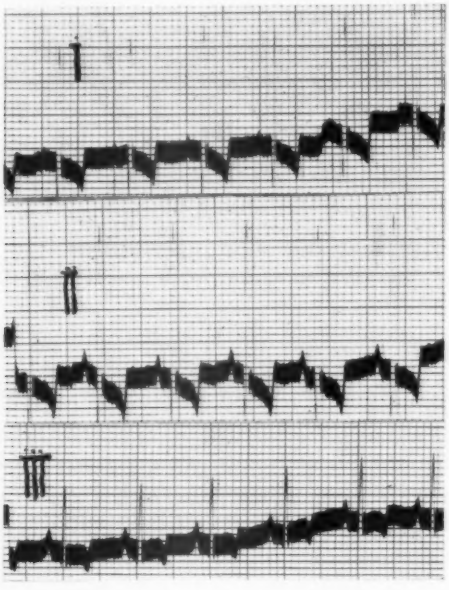

FIG. 14. (DOG K 71.) TWELVE DAYS AFTER 80 MINUTES OF X-RAY, SHOWING PRONOUNCED T WAVE INVERSION IN ALL LEADS

In the three cases in human beings reported by us no electrocardiographic tracings had been made.

In the five sheep, all of which died within a month from pulmonary oedema and cardiac insufficiency, the electrocardiographic changes were not striking and were limited to a more or less pronounced inversion of the T waves in one or more leads with an occasional, relatively insignificant prolongation of the conduction time.

Dogs proved more satisfactory for this type of study. At the time the electrocardiographic tracings were made no morphine was used and the dogs were not anaesthetized. A practically uniform effect among these animals within the first month or two proved to be T-wave inversion. This was commonly quite deep, and present in all three leads. In a few cases the inversion was limited to lead I or in I and II, rarely in II and III.

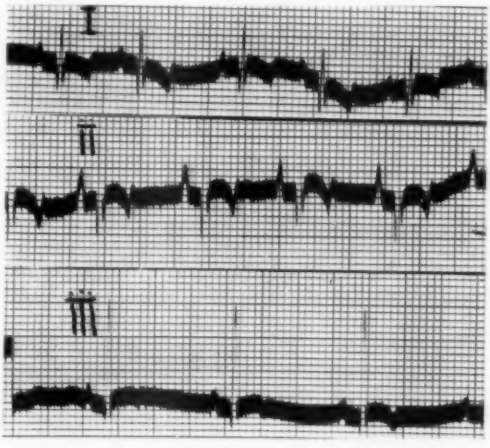

FIG. 15. (DOG H 72.) RECEIVED 40 MINUTES OF X-RAY ON NOVEMBER 8, 1926. ELECTROCARDIOGRAM TAKEN 15 MINUTES AFTER THE X-RAY EXPOSURE SHOWS DEEPLY INVERTED T WAVES IN ALL LEADS

In leads II and III the T waves have a slightly upward convexity such as has been described by Pardee in some cases of coronary artery occlusion.

Since it is agreed by most workers that in its direction and form T is much less stable than are the initial deflections, not too much importance is attached to this alteration. However, it was noted that in some of the dogs submitted to successive x-ray treatments marked T-wave inversion often followed the first treatment, but during the course of a month changed to a flattening of T, only to have again a deep T-wave inversion appear after the second x-ray treatment (Fig. 14). In two instances abnormal forms of T were encoun-

tered similar to those which have been previously described by Pardee (8) and thought to be indicative of coronary artery obstruction (Fig. 15). In one case the T waves were sharply inverted in all leads but the S-T interval displayed a distinct upward convexity in

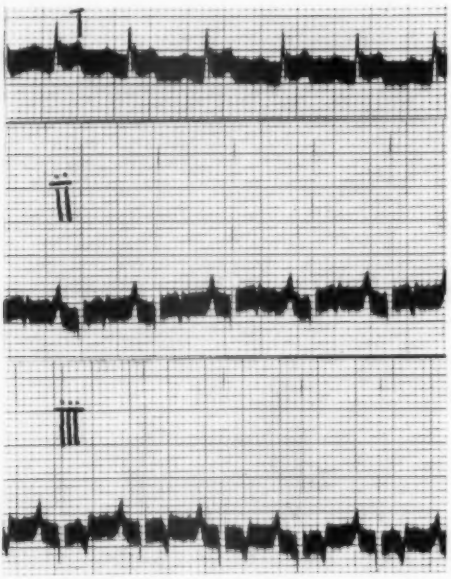

FIG. 16. (DOG H 73.) RECEIVED 80 MINUTES OF X-RAY ON DECEMBER 17, 1926. ELECTROCARDIOGRAM TAKEN APRIL 19, 1927 SHOWS IN ADDITION TO INVERSION OF TIN LEADS II AND III, AN ABNORMAL T WAVE IN LEAD I IN THAT THE S-T INTERVAL BRANCHES OFF FROM THE QRS GROUP SOMEWHAT ABOVE THE BASE LINE OF THE RECORD

This change is similar to that noted in experimental and clinical cases of coronary artery occlusion.

leads II and III, terminating in a sharply hooked inverted T. In the other case in lead I the S-T interval came off from the QRS group at a level distinctly higher than the base line, and this change represented a distinct difference from the electrocardiogram taken on this animal a few weeks previously (Fig. 16).

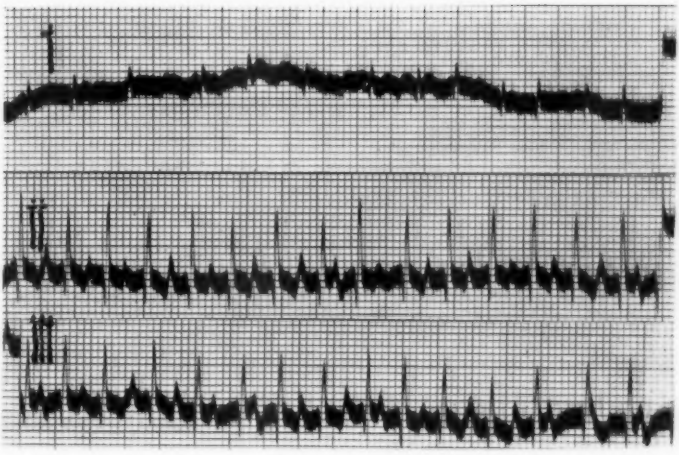

FIG. 17. (DOG P 74.) RECEIVED 145 MINUTES OF X-RAY IN NINE SMALL DOSES FROM JUNE 16, 1926, TO AUGUST 7, 1926. ELECTROCARDIOGRAM TAKEN OCTOBER 8, 1926, SHOWS PROLONGED P-R INTERVAL VARYING FROM 0.12 TO 0.2 SECOND

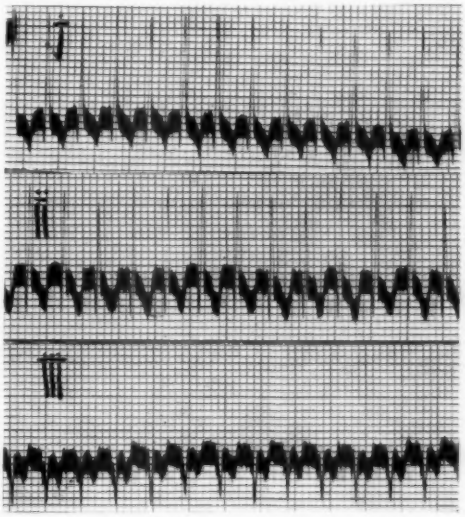

FIG. 18. (DOG G 75.) RECEIVED A TOTAL OF 135 MINUTES OF X-RAY IN FOUR DOSES FROM SEPTEMBER 27, 1926, TO NOVEMBER 13, 1926. ELECTROCARDIOGRAM TAKEN DECEMBER 27, 1926, SHOWS TACHYCARDIA WITH A RATE SLIGHTLY IN EXCESS OF 300 PER MINUTE

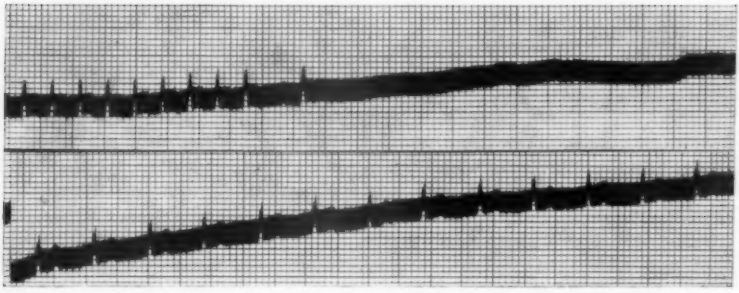

FIG. 19. (DOG L 78.) SHOWING EFFECT OF VAGUS PRESSURE ON PAROXYSMAL TACHYCARDIA

Original rate 345. Rate after vagus pressure 175. (Lead II).

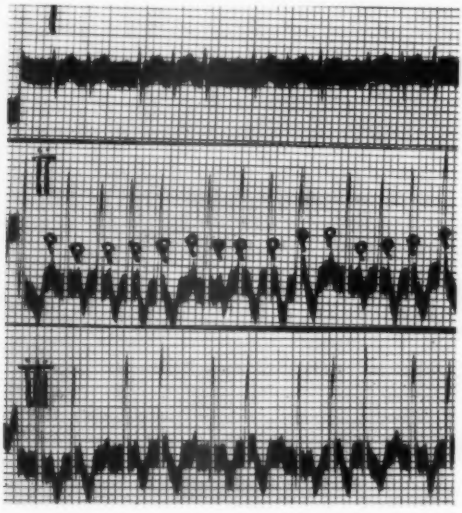

FIG. 20. (DOG H 76.) RECEIVED 75 MINUTES OF X-RAY ON JANUARY 6, 1927, AND 90 MINUTES ON MARCH 14, 1927. ELECTROCARDIOGRAM TAKEN APRIL 21, 1927, SHOWS AURICULAR FLUTTER—AURICULAR RATE OF 390 PER MINUTE WITH A VENTRICULAR RATE OF APPROXIMATELY 270

The response of the ventricle is decidedly irregular.

Another relatively early effect was that of slight enlargement of the P waves, particularly in lead II, but the form and sign of the P waves were not often altered. There was apt to be present also at this period a moderate increase in the voltage of the QRS complexes in leads II and III.

The conduction time, or P-R interval, was occasionally slightly prolonged, for example, from 0.10 or 0.12 to 0.14 or 0.18 seconds. Often, however, the P-R interval was not materially altered from start to finish of the experiments (Fig. 17).

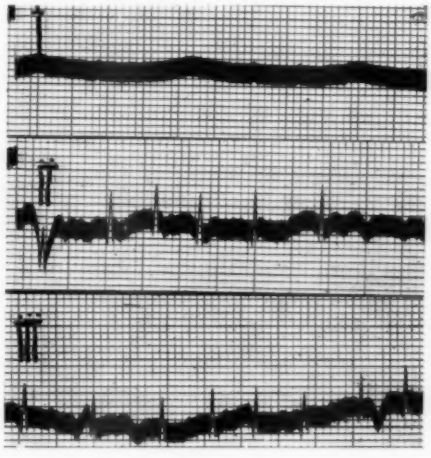

FIG. 21. (DOG G 75.) RECEIVED A TOTAL OF 135 MINUTES OF X-RAY IN FOUR DOSES FROM SEPTEMBER 27, 1926, TO NOVEMBER 13, 1926. ELECTROCARDIOGRAM TAKEN JANUARY 12, 1927, SHOWS AURICULAR FIBRILLATION AND SOMEWHAT LOWER QRS VOLTAGE THAN WAS NOTED IN PREVIOUS CURVES

During the second month or after, consistent increases in rate were apparent. At first these were simple sinus tachycardias with rates of 140 to 160. Later these gave way in some animals to ectopic rhythms of more rapid rates, from 300 to 345 (Fig. 18). It has been difficult from inspection of these records to identify clearly the type of tachycardia on account of the extreme rapidity and the fact that vagus pressure was not used. It is possible that in this group there

may be instances of auricular flutter. However, we have recorded the effect of vagus pressure on one dog that showed a tachycardia with a ventricular rate of 345 (Fig. 19). The effect of vagus pressure in this case is seen to be a ventricular standstill without any preliminary slowing such as is generally met with in auricular flutter, and the standstill does not reveal any evidence of auricular activity. The rhythm was resumed at about one-half the rate shown during the

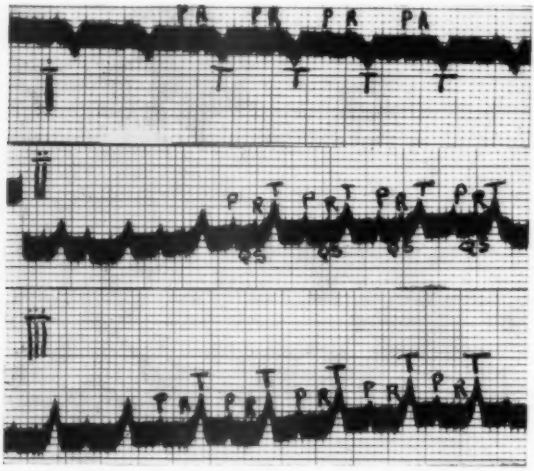

FIG. 22. (DOG B 77.) RECEIVED A TOTAL OF 190 MINUTES OF X-RAY IN THREE DOSES FROM DECEMBER 22, 1926, TO MARCH 19, 1917. ELECTROCARDIOGRAM TAKEN APRIL 27, 1927, SHOWS EXTREMELY LOW QRS VOLTAGE

T waves are sharply inverted in lead I.

tachycardia and the heart did not return to the original rate. For these reasons it seems justifiable to conclude that in this instance the rapid rate was due to paroxysmal tachycardia. Such rapid auricular rates as these, it long continued, would be likely to give rise to some irregularity or lengthening of the refractory period, with varying conduction in the auricular myocardium, thus paving the way for the development of auricular flutter or auricular fibrillation.

We were able to record auricular flutter in four dogs. One example

(Fig. 20) manifests a perfectly regular auricular rate of 390 per minute, while the ventricular responses are distinctly irregular and at a considerably lower rate. Lewis, Feil and Stroud (9) limit the term auricular flutter in the dog to a coördinated and absolutely regular beating of the auricles at rates varying from 340 to 580 per minute. They were able to produce this abnormal rhythm by stimulating the auricle with a rapid series of induction shocks or with a weak faradic current. In a few animals Lewis (10) has been able to induce flutter by injecting glyoxyllic acid into the blood stream. In another of our dogs auricular fibrillation occurred and continued over a period of ten days, after which the animal was sacrificed (Fig. 21). This arrhythmia has previously been encountered in dogs by many observers as an after-effect of faradization of the auricle. It has also been observed as a spontaneous development in horses (11) suffering from cardiac disease, and much more rarely in the dog (12) under similar circumstances. But we have been unable to find record of its production experimentally in the dog in any other way than by direct faradization of the auricle.

All of the dogs that developed auricular flutter and auricular fibrillation after exposure to deep x-ray showed at autopsy extensive hemorrhagic infiltration throughout the right auricle.

The preponderance, as indicated in the electrocardiograms of these dogs and which was not clearly right or left at the start of the experiments, in a few animals became very pronouncedly a right preponderance toward the later months of the study.

In only one animal, which was rayed entirely through the right side of the chest, was any abnormality of the QRS complexes noted. In this dog a few days before death a curve was obtained which showed these complexes to be very small, almost isoelectric. Autopsy on this dog showed not only very pronounced damage to the right ventricular myocardium but also to the intraventricular septum (Fig. 22).

SUMMARY

1. The effect of carefully measured irradiation upon the heart of the experimental animal (sheep, dog) has been studied, clinically and pathologically. If the dosage is sufficient, either in a single massive or in often repeated smaller applications, certain characteristic pathological changes are brought about in the heart.

2. The gross changes are as follows: (*a*) Hydropericardium. (*b*) Hemorrhagic infiltration of the right auricle, especially of the right auricular appendage. (*c*) More rarely, after heavy dosage has been projected through the side, there is thickening and hyaline degeneration of the epicardium with hemorrhagic infiltration of the ventricular walls. (*d*) At autopsy these animals show passive congestion of the viscera.

3. Certain characteristic microscopical changes in the heart have been described: (*a*) in the auricular myocardium, (*b*) in the ventricular myocardium, (*c*) in the His bundle of the sheep.

These microscopic myocardial changes vary with the acuteness or chronicity of the lesions produced.

4. The records are presented of patients who were given relatively large amounts of deep x-ray over the cardiac area as a therapeutic measure for mediastinal or lung tumors, and who later came to autopsy. Microscopical sections of the myocardium from these patients show changes which are comparable to those found in the experimental animal following exposure to x-ray, but the terminal infection in the first and third cases and the age of the second patient may have a bearing on the findings.

5. Electrocardiographic records made from the different dogs used in the experiments reported showed a variety of deviations from the normal, more noteworthy changes being: (*a*) Inversion of T in leads I and II and frequently in III as well. Certain abnormal forms of T. (*b*) Paroxysmal tachycardia. (*c*) Auricular flutter was recorded in four animals. (*d*) Auricular fibrillation was recorded once. (*e*) Slight prolongation of the P-R interval. (*f*) Diminished QRS voltage.

CONCLUSIONS

1. In the experimental animal ample evidence has been presented, from the standpoint of pathology and electrocardiography, that injury to the heart results from the direction of deep x-ray over it in sufficient dosage.

2. That the myocardium in man is also susceptible to the effects of the deep x-ray is indicated by the findings noted in the three human cases reported.

3. The deep x-ray offers a new non-operative method of producing experimentally the myocardial lesions and the electrocardiographic abnormalities reported.

4. Auricular fibrillation and auricular flutter in the dog experimentally produced in a non-operative manner and without the use of drugs or anaesthetics have been recorded.

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A STUDY OF THE OVARIAN FOLLICULAR HORMONE IN THE BLOOD OF THE PREGNANT WOMAN[1]

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A short time ago it was shown by the author that pregnancy in the rat could be interrupted by an extract of ovarian follicular fluid if it were given in sufficient amounts in the early part of pregnancy. This finding has been confirmed by the work of Parkes and Bellerby. Also, there can be demonstrated in the placenta a substance which exerts the same effect upon the vaginal mucosa of the ovariectomized rat as does the ovarian follicular hormone and is therefore most probably identical with that hormone; and further, Frank and Goldberger have shown that while the blood of non-pregnant women contains an active substance possessing quite similar properties, the blood of women in the early months of pregnancy contains much more of it than does the blood of normal women. Because of the apparent inconsistency between the fact that injections of the follicular hormone can terminate pregnancy in the rat and the demonstration of its presence in high concentration in the blood of pregnant women, the present study was undertaken in order to investigate in more detail the quantitative occurrence of this substance in the blood of pregnant women.

During the progress of this work similar investigations have been reported by Fels and by Ascheim.

Extracts of blood in varying dilutions from a large number of women at different stages of pregnancy have been tested for the follicular hormone. Only those cases are considered here in which a definite menstrual history was given by the patient, that is, the exact date of the onset of the last period, or in which the probable duration of pregnancy was later checked by the date of delivery. In spite of the chance for error in the calculation of the duration of pregnancy,

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in the variability of the test animals, and in the extraction of the blood, the results have been quite uniform.

TECHNIQUE

Through the courtesy of the members of the obstetrical staff and especially of Dr. Dorothy Loynes I was able to obtain specimens of blood for this work.

TABLE I

Showing the amount of blood in which the follicular hormone can be demonstrated at different periods of pregnancy

The amounts are expressed in cubic centimeters

SIXTH WEEK		SECOND TO THIRD MONTH		THIRD TO FOURTH MONTH		FOURTH TO FIFTH MONTH		FIFTH TO SIXTH MONTH		SIXTH TO SEVENTH MONTH		SEVENTH TO EIGHTH MONTH		EIGHTH TO NINTH MONTH		NINTH TO TENTH MONTH		DURING LABOR AND SHORTLY BEFORE ITS ONSET	
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0
50	–	34	–	20	–	33	–	33	–	20	–	20	–	36	–	35	–	1.25	0.625
50	–	33	–	20	15	33	–	27	–	5	2.5	27	–	31	–	34	–	1.25	0.625
		31	–	15	–	31	16	19	–	5	2.5	30	–	31	–	20	–	1.25	0.625
		31	–	15	–	20	15	10	5	5	2.5	23	–	20	–	10	–	1.25	0.625
		35	–	–	15	–	15	10	5	5	2.5	5	2.5	20	–	5	2.5	1.25	–
		–	30			–	15	5	2.5	5	2.5	5	2.5	19	–	5	2.5		
		–	35			15	–	5	2.5	5	2.5	5	2.5	10	–	5	2.5		
		–	30			15	10	2.5	1.25	5	2.5	5	2.5	5	2.5	–	5		
						10	–			2.5	–			2.5	1.25	5	2.5		
						10	5									2.5	1.25		
						5	–									2.5	1.25		
						5	2.5									2.5	1.25		
																2.5	1.25		

A measured amount of blood taken from an arm vein was received into twice its volume of 95 per cent alcohol. After filtration the precipitate was washed several times with 95 per cent alcohol. It was allowed to dry in the air and was then extracted three times with ether. In each extraction a volume of ether equal to about three times the volume of the precipitate was used. The alcohol filtrate and the washings were also evaporated to dryness and extracted with ether. The combined ether extractions were

evaporated to dryness and the residue was dissolved in 95 per cent alcohol. This solution therefore contained the entire amount of follicular homone extracted from the measured specimen of blood. It was divided into portions in order to obtain the amount of substance representing varying amounts of blood. The alcohol was evaporated from each portion and each residue emulsified in about 1 cc. of distilled water. This was injected subcutaneously in three parts at intervals of three to four hours.

TABLE II

Amount of postpartum blood required to demonstrate the follicular hormone

AMOUNT OF BLOOD EXTRACTED	7 HOURS	10 HOURS	14 HOURS	21 HOURS	36 HOURS	2 DAYS	3 DAYS	4 DAYS
cc.								
35				+	0	0	0	0
20		+		0				
15				0				
10	0		0					

TABLE III

Comparison of the concentration of the follicular hormone in the maternal and the cord blood and in the placenta

Smallest amounts required to give a positive result

PLACENTA	MATERNAL BLOOD	CORD BLOOD
grams	*cc.*	*cc.*
0.5 +, 0.25 ±	1.25 +	1.25 +
0.5 +, 0.25 ±	1.25 +	1.25 +
0.5 +, 0.25 ±	1.25 +	1.25 +

The change produced in the vaginal smears of ovariectomized mice was used to test the extracts. Whenever possible, a dilution of blood which gave a negative result was checked by a duplicate injection in another mouse. This was not always possible when the amount of blood required to give a positive result was large.

From the beginning of pregnancy to the onset of labor there is a continual increase in the concentration of the ovarian follicular hormone in the blood. The most striking increase occurs between the first and sixth months but the concentration continues to increase

until the end of pregnancy. A few days before the onset of labor there is a final rise in the concentration which persists during labor. This proceeds about as follows:

At the sixth week after the onset of the last menstrual period a slight but definite change is produced in the appearance of the vaginal smear in ovariectomized mice by the injection of the extract from 50 cc. of blood. Fifty cubic centimeters of the blood of non-pregnant women has not given this effect. During the sixth month of pregnancy the extract from only 5 cc. of blood will sometimes give a definite change, while more than this always does so. Late in pregnancy only 2.5 cc. are required to obtain a positive result. A positive result has not been obtained by this method with less than 2.5 cc. except during labor and within a few days of its onset. At this time positive results were always given by the equivalent of as little as 1.25 cc. of blood. It is of course possible that these actual amounts would vary with the use of different methods of extraction, but these results give at least the relative concentrations of the substance at different periods of pregnancy.

The accompanying tables will show in detail this increase in concentration as pregnancy advances.

In three cases not only the maternal blood, during labor, but also the placental and the cord blood were tested. In these three cases identical results were obtained. In the maternal and cord blood the concentration of the follicular hormone was the same, the 1.25 cc. dilution being the lowest which gave a positive result. A representative piece of each placenta, weighing betwen 15 and 20 grams, was extracted and in each instance a positive result was obtained from 0.5 gram of placenta, and a doubtful result with 0.25 gram, showing apparently that this substance exists in higher concentration in the placenta than in either the foetal or maternal blood. The significance of this apparent high concentration in the placenta was not investigated further.

Immediately after labor the concentration of the follicular hormone drops with great rapidity. Seven hours after labor it cannot be demonstrated in 10 cc. of blood, while 24 hours after it can be demonstrated in 35 cc. of blood but not in 20 cc.; and after twenty-four hours it cannot be demonstrated in 35 cc. of blood. It has been demonstrated

in catheterized specimens of urine taken late in pregnancy, as well as after delivery. No difference could be demonstrated in the rate of its excretion shortly before labor and within the six hours immediately following labor.

CONCLUSIONS

The concentration of a substance, identical in its biological property with the ovarian follicular hormone, increases in the blood of pregnant women from the onset to the termination of pregnancy.

It has always been found in the same concentration during and shortly before labor and its concentration at this time is greater than that found at any other time.

There is an immediate rapid disappearance of this substance from the blood following delivery. It can be demonstrated in the urine before and following labor.

The amount found in the placenta per gram of weight is approximately twice that found in the blood per cubic centimetre.

The concentration in the maternal blood during labor and in the blood from the cord is the same.

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BOOK REVIEWS

The Modern Practice of Pediatrics. By William Palmer Lucas. 922 pp. $8.50. (*The Macmillan Co., New York, 1927.*)

The professed aim of Dr. Lucas's book is not only to cover the "orthodox" field of pediatrics, but to relate the study of disease to the positive aspects of health. Thus we find in the volume a considerable amount of material devoted to public health. An excellent résumé of the history of preventive pediatrics is followed by a somewhat extensive discussion of prenatal care. Later on, there are many pages devoted to details of normal diets, illustrations of posture standards, suggestions for teaching health, etc. A chapter on "The Protective Value of 'The Newer Knowledge of Nutrition'" bears witness to the author's purpose of showing "how the most technical, the most intricate problems of the research laboratory . . . . are related, in their contribution and significance to the prevention of disease." It is essentially an essay on the value of animal experimentation in the study of nutrition, and might well be enlightening to a layman, although it seems doubtful if the idea will be a new one to the third year medical student or the practitioner. Passages like the following give further evidence of the author's zeal for public health: "The goal" [in the treatment of bronchitis] "is normal sound health. Physicians must recognize the social aspects of their profession. Life is to be saved, disease is to be diagnosed, treated and cured when possible, scientific medical research is to be constantly fostered, and positive health is to be sought and achieved by health education, and it is all to be related to that great shadowy mass of human beings known as 'the public.'"

When one turns to presentation of the "orthodox" field of pediatrics it is difficult to escape the impression that the sick child has suffered at the expense of the well one. The field is extensively covered; indeed there are descriptions of many conditions not ordinarily included in textbooks of pediatrics: fractures, burns, accidents, major psychoses, and others. The more "orthodox" topics are usually given a conventional treatment, but the discussions of the fundamental pathology of disease are at times inadequate. Symptoms of disease are often listed numerically in order of their frequency, but the clinical descriptions are inclined to be brief and lacking in vividness. It would seem that the Bokay prophylactic treatment for corrosive stricture of the esophagus deserved mention in a work emphasizing preventive medicine.

The number of inaccuracies which have escaped the proof reader seems unduly large. One can quite readily forgive the mention of a certain organism as the "Moron Axonfeld" bacillus; likewise the information vouchsafed under "vulvovaginitis" that "the vast majority of cases occur in girls," although "the symptoms in boys are much the same." But statements like the following are less easy to

excuse: the prognosis of pneumonia "with types I and III is the most serious, as there is as yet no specific for these types. Type II is just as virulent an organism as type I, but fortunately there is a specific anti-serum which, if given early, reduces the mortality."

The discussion of the physiology of the infant is, in the main, good. Mention is made of the "molability" of enzymes, whatever that obscure property may be. The Cannon theory of the closure of the pylorus is given unchallenged, despite the fact that many infants with acid duodenal contents appear to have no difficulty with their pyloric function. The statement that HCl therapy may lead to "acute acidosis," so that one should watch the urine for acetone and diacetic acid, seems hardly in accord with accepted ideas of the origin of ketosis.

Dr. Lucas's book is, however, clearly and forcefully written. It is rendered more readable by the short historical paragraphs included with many diseases, and, not the least noteworthy feature, one which might well be copied by other contemporary texts, is a bibliography at the end of each chapter.

L. E. H.

The Pathology and Treatment of Diabetes Mellitus. By GEORGE GRAHAM. Second edition. 230 pp. $2.75. (*Humphrey Milford, Oxford University Press, London, 1926.*)

Graham's Pathology and Treatment of Diabetes Mellitus has grown up from the Goulstonian lectures given by him in 1921. It can, therefore, claim to be distinguished from the flood of literature which has followed the isolation of insulin. In 1915 the author arrived at a method of treating diabetes similar to that of Allen in this country, although he approached the problem from another angle. After the war, further experience warranted the publication of his thesis and results. Before the books was fully written, insulin became available. At the time of the first edition (1923), the possibilities of this new means of treatment were still being explored and it was discussed rather independently of the methods that had been tested out and found useful. The present edition contains the results of a much fuller experience in the use of insulin combined with dietetic treatment.

Of the three main schools of thought in the treatment of diabetes, Dr. Graham has ever been one of the most vigorous proponents of that which considers that the fasting blood sugar should be brought and kept within normal limits. Even to those who have arrived at other conclusions, the restatement of the premises on which his opinion is based can have nothing but value. The lessons learned in the preinsulin days are not discarded and insulin is regarded as an aid to rather than a substitute for treatment by diet ". . . . the discovery of insulin has not altered the main principle of treatment, which can be restated as follows. The blood sugar in the fasting state should be within the normal limits of 0.08 to 0.13 per cent, and should rise above this level only for short periods after meals. Insulin has enabled this ideal to be achieved with much greater ease. . . . ."

The account of the physiology of the sugar-regulating mechanism and of such facts as are known of the pathology of diabetes makes interesting reading. The

discussion of the various forms of innocent glycosuria, with which the author has had considerable experience, forms a valuable addition to the literature of the subject. Dr. Graham and his publishers have been very modest in the reproduction of the charts throughout the book and some are a little difficult to decipher. It is, perhaps, in the eight appendices that he who is confronted with a diabetic patient will find the most practical assistance. Diets, laboratory methods and scales of insulin dosage are conveniently collected there. Many longer books on diabetes have been written; none have given a more lucid and helpful account of the pathology and treatment of the disease.

C. F. H.

History Taking and Recording. By JAMES A. CORSCADEN, M.D. 78 pp. $1.50. (*Paul B. Hoeber, New York, 1926.*)

A well conceived little book designed to assist in the proper recording of an anamnesis. A comprehensive outline is appended to the text. The peculiar merits of this book are: (1) The emphasis placed on the importance of portraying the personality of the patient; (2) the discussion of the manner of describing the "present illness" of the patient, dividing facts obtained into those which have to do with the manner of onset, the course and the present status, respectively; (3) the necessity of including a full delineation of the symptomatology, the absence of symptoms being recorded as well as their presence. The use of the histories for statistical purposes in the study of disease is worthy of special comment.

E. H. H.

Bacteriological Atlas. By RICHARD MUIR. 134 pp. $4.50. (*Wm. Wood and Co., New York, 1927.*)

This little volume contains sixty, full page, beautifully colored plates picturing most of the common pathogenic microorganisms as seen in smears stained by Gram's or other appropriate methods. Each plate is accompanied by a short explanation. As a rule, the organisms are shown in pus or blood.

The pictures appear somewhat idealized, perhaps even diagrammatic. The bacteria seem, in some cases, almost disproportionately enlarged. Also, it must be kept in mind that quite often a dozen pictures would be needed to portray a given organism in all its morphological and tinctorial vagaries. The book is obviously intended for very elementary instruction.

M. F. JR.

The Specialties in General Practice. Compiled by Francis W. Palfrey, M.D. Instructor in Medicine at Harvard University in collaboration with 14 other teachers of Harvard Medical School. 8°. pp. 748. $6.50. (*W. B. Saunders Company, Philadelphia and London, 1927.*)

Increased intricacy in methods of diagnosis and treatment has quite naturally given rise to specialization in certain branches of medicine in which an elaborate technique requires special training or equipment. The family physician has

accordingly assumed a somewhat different position in the household. Much less frequently than formerly is he at once the obstetrician, the pediatrician, the dermatologist, the psychiatrist, and the surgeon as well as the medical consultant of the family. At present his rôle outside of the field of internal medicine is coming to be that of medical adviser. As the family physician, he is still usually the first to be consulted when any member of the household is ailing, but if the condition clearly lies in the field of a specialty, he is not expected to treat it except in an emergency. These emergencies are of sufficient frequency, however, to make it necessary for the internist as well as the general practitioner to be properly equipped to meet them. Naturally, also, this equipment in the form of a general knowledge of the specialties is of great value in diagnosis and in following intelligently the case of a patient who is being treated by a specialist.

Too often the general practitioner, in seeking light on some simple clinical problem outside of his own field, is confronted with exhaustive treatises which merely confuse him. What he wants is a concise and practical exposition of the common conditions, their diagnosis and treatment. In many cases, indeed, he merely needs to be reminded of what he has once learned and has perhaps forgotten. This long-felt need has been adequately filled in Dr. Palfrey's book. In collaboration with fourteen specialists, all of whom are on the teaching staff of the Harvard Medical School, he has presented in a very able way what the general practitioner should know about the specialties. The book is divided into eleven sections, each devoted to one of the special branches. His collaborators are men who speak with authority, but the practical viewpoint of the attending physician has never been lost sight of. The chapter on sexual hygiene is the sanest exposition we have seen of a vital problem which has been side-stepped by most medical schools.

J. M. F.

Basal Metabolism in Health and Disease. By EUGENE F. DUBOIS. Second edition. 421 pp. (*Lea and Febiger, Philadelphia, 1927.*)

The need for this treatise is demonstrated by the appearance of a second edition, carefully brought up to date, three years after the first publication. The author has mastered in all its details the great mass of metabolic and calorimetric work that has been one of the outstanding features of scientific endeavor on this continent in recent years. He is, perhaps, better fitted to interpret the subject of Basal Metabolism for "those engaged in the practice of medicine and surgery, for medical students, for physiologists and for dietitians" than any one else who has engaged in this work. A very welcome change is found in the arrangement of the subject matter dealing with normal metabolism and selection of standards. In the first edition one looked in vain for the familiar Sage Institute Curve in the chapter on "Normal Basal Metabolism," and the lack of it was a source of confusion to anyone not familiar with the development of the subject. In the new edition, however, this chapter includes excellent graphs of all the better known scales of normal basal metabolic values. A new chapter on "The selection of

Normal Standards'' is very helpful. The book maintains an easy lead over similar monographs and supplies a much needed source of authoritative information on this rapidly developing subject.

J. T. K., Jr.

The Treatment of Fractures. By Charles Locke Scudder. Tenth edition revised, with 2027 illustrations. 1240 pp. $12.00. (*W. B. Saunders & Co., Philadelphia and London, 1926.*)

This tenth edition is far more complete than its forerunners, and contains nearly 500 additional pages, which are taken up with the discussion of subjects not included before. The chapter on "Bone Repair" by Bancroft deserves special comment. This is an extremely clear and orderly presentation of the subject with beautiful illustrations. Ununited Fractures are taken up in several chapters. All of the latest experimental work is discussed, and an excellent summation of this interesting problem is given. Pathological Fractures are well discussed by Bloodgood and Birth Fractures by the Author. The chapters on bone grafting and special operations should prove most helpful to practising surgeons, and give the student a good clear idea of these problems in bone work. Other new chapters deal competently with the conduct of open operations on fractures, the methods of fixation of fractures, the surgical approach to bones, compound fractures, massage and the relation of the Surgeon to the Law.

The main portion of the book is also more complete than in the previous editions. There are separate chapters on extension and counter-extension, skeletal traction, and peripheral nerve injuries associated with fractures. Special note should be made of the detailed description of the U. S. A. Balkan Frame, and Langworthy's apparatus for the treatment of fractures of the femur. A good deal of space is given to the Delbet Method for treating fractures of both bones of the lower leg, a method little used in this country, but which has given excellent clinical results. The chapter on the x-ray relationship to fractures has been omitted from this edition.

Many additional illustrations render this edition more valuable to the student in visualizing the subject. The text proper is somewhat fuller, and is not overcrowded with details of treatment. More attention is paid to the gross anatomy and to the mechanical forces involved in fractures, which are so often lost sight of. It is certainly a good book which one handling fractures should have for reference, and an excellent textbook for students.

A. R. S.

Principles of Physical Chemistry for Medical Students. By Phillis M. Tookey Kerridge. 134 pp. $1.75. (*Oxford Medical Publications. Oxford University Press, London, 1927.*)

As the author states in her preface, "the purpose of this little book is utilitarian." It is primarily designed to give the English medical student a brief "outline of some of the principles of physical chemistry which have been of great service for appli-

cation to physiological and medical problems," and is based upon the short lecture and laboratory course which the author has given under Prof. A. V. Hill at University College in London. So small a book can scarcely be called a text of physical chemistry; it is rather a compendium which a student may find useful in conjunction with a more elaborate lecture course. The more important principles of the orthodox physical chemistry, as well as some of the more recent topics applicable to biology, such as colloids, catalysis and hydrogen-ion concentration, are very clearly and simply stated, and illustrative examples of physiological phenomena are well chosen. But after a perusal of this booklet one is left with a distinct regret that the author has chosen so compressed a mode of presentation, since a somewhat greater expansion of the explanatory text, even without an enlargement of the scope of the book, would have permitted the student to assimilate the facts and theories presented with greater facility and perhaps more thoroughly. The same may be said of the small number of practical laboratory experiments appended at the end.

W. A. P.

Mother and Unborn Child. A Little Book of Information and Advice for the Prospective Mother. By SAMUEL RAYNOR MEAKER, Associate Professor of Gynecology, Boston University School of Medicine. 209 pp. with 22 illustrations. $2.50. (*Williams & Wilkins Company, Baltimore, 1927.*)

This book, intended as a guide for the expectant mother, is written in a simple, interesting style and the author is to be congratualted on the sympathetic attitude that pervades his volume. While in general the advice offered is sound and conservative, it is doubtful if explanations and discussions of Caesarean section, forceps and other obstetric operations should be included in a book planned for the expectant mother. Likewise, one is led to wonder if such explicit directions concerning the preparation of the patient for delivery, the choice of anaesthetics, the use of abdominal binders and other such subjects concerning which obstetricians are rarely in accord, do not tend to confuse rather than aid the reader.

A recent bibliography lists more than eighty books that have been published in this country within the past ten years on prenatal care and the care of the baby. One wonders if the field is not becoming adequately covered.

J. W. H.

BOOKS RECEIVED

Actions and Uses of the Salicylates and Cinchophen in Medicine. By P. J. HANZLIK, M.D. Medicine Monographs, volume IX. 1927. 8°. 200 pages. The Williams & Wilkins Company, Baltimore. $3.50.

De Lamar Lectures 1925–1926. By DAVID MARINE, ALICE HAMILTON, FRANCIS CARTER WOOD, [*et al*]. The Johns Hopkins University School of Hygiene and Public Health. 1927. 8°. 220 pages. The Williams & Wilkins Company, Baltimore. $5.00.

Early Days of the Presbyterian Hospital in the City of New York. By DAVID BRYSON DELAVAN, M.D. With 34 full page illustrations. 1926. 8°. 191 pages. Published privately.

Pernicious Anaemia, Leucaemia and Aplastic Anaemia. An Investigation from the Comparative Pathology and Embryological Point of View. By J. P. MCGOWAN, M.A., M.D., B.Sc. With twelve illustrations, including two coloured. 1927. 8°. 116 pages. Paul B. Hoeber, New York. $3.00.

Mother and Unborn Child. A Little Book of Information and Advice for the Prospective Mother. By SAMUEL RAYNOR MEAKER. 1927. 8°. 209 pages. The Williams & Wilkins Company, Baltimore. $2.50.

Infections of the Hand. By LIONEL R. FIFIELD, F.R.C.S.Eng. With 2 coloured plates and many other illustrations. 1927. 12°. 192 pages. Paul B. Hoeber, New York. $3.00.

Hospital Housekeeping and Sanitation. By NORA P. HURST, R.N. 1926. 24°. 155 pages. The C. V. Mosby Company, St. Louis. $1.25.

A Manual in Preliminary Dietetics. By MAUDE A. PERRY, B.Sc. 1926. 16°. 146 pages. The C. V. Mosby Company, St. Louis. $1.25.

A Primer for Diabetic Patients. A Brief Outline of the Treatment of Diabetes with Diet and Insulin, Including Directions and Charts for the Use of Physicians in Planning Diet Prescriptions. By RUSSELL M. WILDER, M.D. Third edition, reset. 1927. 16°. 134 pages. W. B. Saunders Company, Philadelphia and London. $1.50.

Pediatrics. Edited by Isaac A. Abt, M.D. With the collaboration of William I. Fishbein, M.D. The Practical Medicine Series, comprising eight volumes on the Year's Progress in Medicine and Surgery. Under the General Editorial charge of CHARLES L. MIX, A.M., M.D. Series 1926. 12°. 381 pages. The Year Book Publishers, Chicago. $2.25.

A Textbook of Bacteriology. A Treatise on the Application of Bacteriology and Immunology to the Etiology, Diagnosis, Specific Therapy and Prevention of Infectious Diseases for Students and Practitioners of Medicine and Public Health. By HANS ZINSSER, M.D. With a section on Pathogenic Protozoa by E. E. TYZZER, A.M., M.D. (Rewritten, revised and reset). With 181 illustrations in the text. Sixth edition. 1927. 8°. 1053 pages. D. Appleton and Company, New York. $7.50.

Nursing Mental and Nervous Diseases. From the View-Points of Biology, Psychology and Neurology. By ALBERT COULSON BUCKLEY, M.D. 57 illustrations. Lippincott's Nursing Manuals. 1927. 8°. 312 pages. J. B. Lippincott Company, Philadelphia. $3.00.

This Business of Operations. By JAMES RADLEY. Foreword by J. M. Withrow, M.D. 1927. 16°. 96 pages. The Digest Publishing Company, Cincinnati.

Outlines of Common Skin Diseases. Including Eruptive Fevers. By T. CASPAR GILCHRIST, M.D. Also diet plans for children. 1927. 8°. 54 pages. The Williams & Wilkins Company, Baltimore.

Piersol's Normal Histology. With Special Reference to the Structure of the Human Body. Thirteenth edition now first edited and in part rewritten by William H. F. Addison, B.A., M.D. 432 illustrations, 32 of which are in color. 1927. 8°. 477 pages. J. B. Lippincott Company, Philadelphia. $6.00.

Immunity in Syphilis. By ALAN M. CHESNEY. Medicine Monographs, Volume XII. 1927. 8°. 85 pages. The Williams & Wilkins Company, Baltimore. $2.50.

Anatomical Texts of the Earlier Middle Ages. A Study in the Transmission of Culture. With a Revised Latin Text of Anatomia Cophonis and Translations of Four Texts. By GEORGE W. CORNER, M.D. 1927. 8°. 112 pages. Published by the Carnegie Institution of Washington.

A Textbook of Exodontia. Exodontia, Oral Surgery and Anesthesia. By LEO WINTER, D.D.S. With 329 illustrations. 1927. 8°. 364 pages. The C. V. Mosby Company, St. Louis, $7.50.

Die Klinik der bosärtigen Geschwülste. Unter Mitwirkung von PROF. DR. A. DÖDERLEIN, PROF. DR. O. FRANKL, [*et al.*] Herausgegeben von Geh. Rat. Prof. Dr. P. Zweifel und Geh. Med.-Rat Prof. Dr. E. Payr. 111. Band. *Brust- und Bauchorgane, Harn- und weiblicher Geschlechtsapparat, Strahlen- und Vakzinebehandlung.* Mit 184 Text-abbildungen und 44 farbigen Tafeln. 1927. 8°. 656 pages. S. Hirzel, Leipzig. 76 Mk.

Gynecological Diagnosis and Pathology. By A. H. F. BARBOUR, M.D., LL.D., F.R.C.P., and B. P. WATSON, M.D., F.R.C.S. Ed., F.A.C.S. Third edition reprinted. With eight colored plates and 201 figures. 1927. 8°. 223 pages. William Wood and Company, New York. $4.00.

Preventive Medicine and Hygiene. By MILTON J. ROSENAU. Fifth edition, 1927. 8°. 1458 pages. D. Appleton and Company, New York and London.

Surgical Applied Anatomy. By SIR FREDERICK TREVES, Bart. Eighth edition, revised by C. C. Choyce, C.M.G., C.B.E., B.Sc. N. Z., M.D. Edin., F.R.C.S. Eng. Illustrated with 162 figures including 66 in colour. 1927. 16°. 727 pages. Lea & Febiger, Philadelphia.

Health Record for Children. By J. THERON HUNTER, M.D. 1927. 8°. 52 pages. The Williams & Wilkins Company, Baltimore.

Clinical Neurology for Practitioners of Medicine and Medical Students. Largely based upon the book by Prof. Dr. Hans Curschmann. (A free translation with changes and additions.) By EDWARD A. STRECKER, A.M., M.D., and MILTON K. MEYERS, B.S., LL.B., M.D. 1927. 8°. 410 pages. P. Blakiston's Son & Co. Philadelphia. $3.50.

Saving Eyesight after Mid-Life. By JOHN HERBERT WAITE, M.D., S.M. Harvard Health Talks. 1927. 24°. 48 pages. Harvard University Press, Cambridge. $1.00.

Health Supervision and Medical Inspection of Schools. By THOMAS D. WOOD, A.M., M.D., and HUGH GRANT ROWELL, A.B., M.D. Illustrated. 1927. 8°. 637 pages. W. B. Saunders Company, Philadelphia. $7.50.

The Elements of General Zoology. A guide to the study of animal biology correlating function and structure, with notes on practical exercises. By WILLIAM J. DAKIN. 1927. 8°. 496 pages. Humphrey Milford, Oxford University Press, London.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A.M., M.D. With the collaboration of Chas. H. Mayo, M.D. Volume 1. Thirty-seventh Series, 1927. 8°. 304 pages. J. B. Lippincott Company, Philadelphia and London. $3.00.

American Gynecological Society. Transactions. Volume 51. For the year 1926. Edited by Arthur H. Curtis, M.D. 8°. 314 pages. St. Louis.

The Anatomy of Science. By GILBERT N. LEWIS. 1926. 8°. 221 pages. Yale University Press, New Haven. $3.00.

The Theory of the Gene. By THOMAS HUNT MORGAN. 1926. 8°. 343 pages. Yale University Press, New Haven. $4.00.

American Ophthalmological Society. Transactions. Sixty-second annual meeting. Volume XXIV, 1926. 8°. 397 pages. Philadelphia.

Basal Metabolism in Health and Disease. By EUGENE F. DUBOIS, M.D. Second edition, thoroughly revised. Illustrated with 92 engravings. 1927. 8°. 431 pages. Lea & Febiger, Philadelphia.

Tuberculosis of the Lungs. A Practical Guide for General Practitioners. By H. HYSLOP THOMPSON, M.D., D.P.H., and A. P. FORD, M.R.C.S., L.R.C.P., D.P.H. 1927. 8°. 179 pages. William Wood & Company, New York, $4.00.

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Self-Care for the Diabetic. For the Use of Diabetic Patients. By J. J. CONYBEARE, M.C., M.D.OXON., F.R.C.P. (Lond.) 1926. 12°. 70 pages. $1.15.

The Treatment of Chronic Deafness by the Electrophonoide Method of Zünd-Burguet. By GEORGE C. CATHCART, M.A., M.D. 1926. 12°. 88 pages. $1.35.

Histological Technique. For Normal Tissues, Morbid Changes and the Identification of Parasites. By H. M. CARLETON, M.A., B.Sc., D.Phil. Chapters VII and VIII in collaboration with Frederic Haynes, B.A. 1926. 8°. 398 pages. $5.00.

Principles of Diagnosis and Treatment in Heart Affections. By SIR JAMES MACKENZIE, M.D., F.R.S., F.R.C.P., LL.D. Ab. & Ed., F.R.C.P.I. (Hon.) and JAMES ORR, M.B., Ch.B. Third edition. 1926. 8°. 242 pages. $3.50.

The Psycho-Pathology of Tuberculosis. By D. G. MACLEOD MUNRO, M.D., C.M., M.R.C.P. (Ed.) 1926. 8°. 92 pages. $1.75.

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